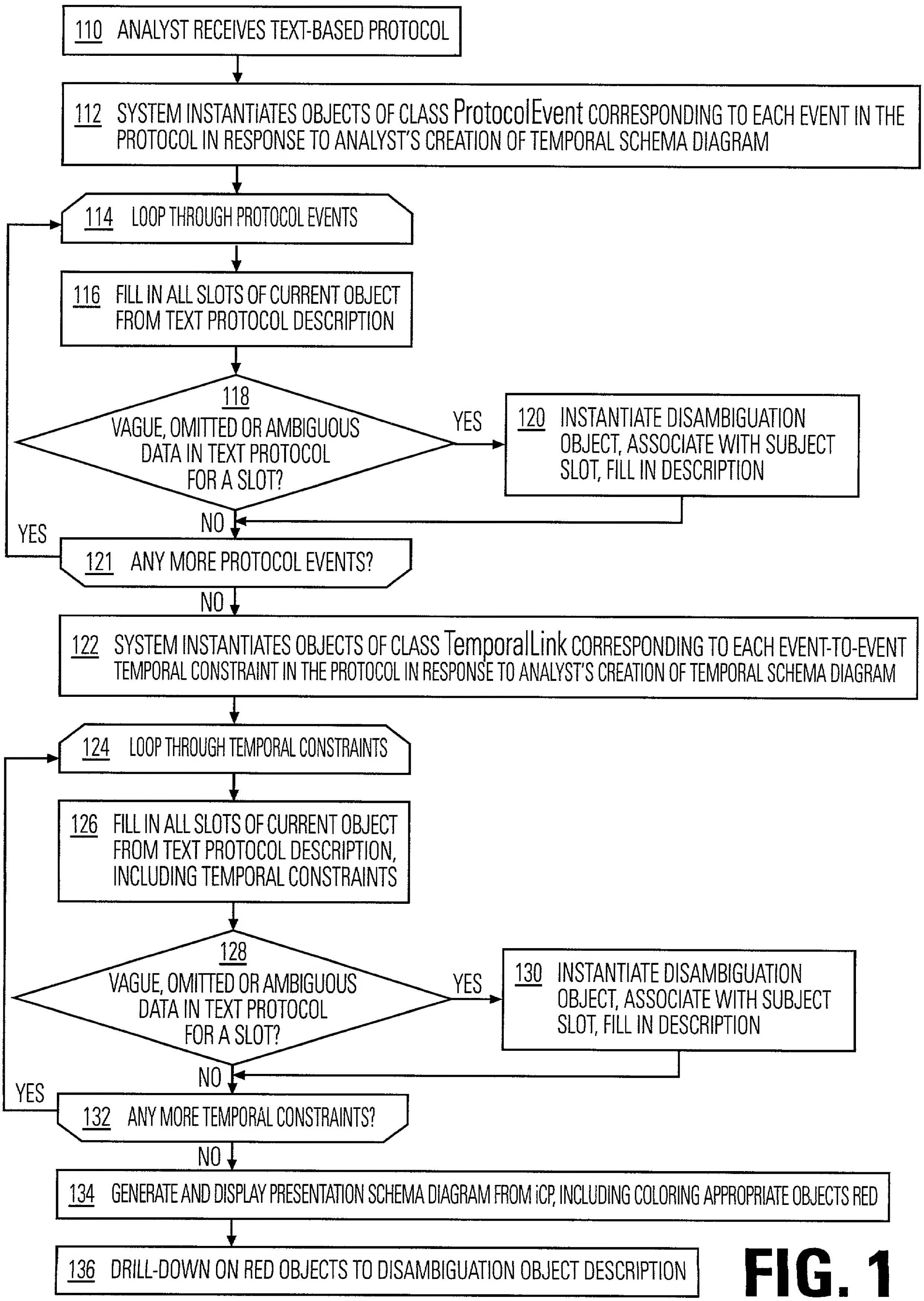


FIG. 1

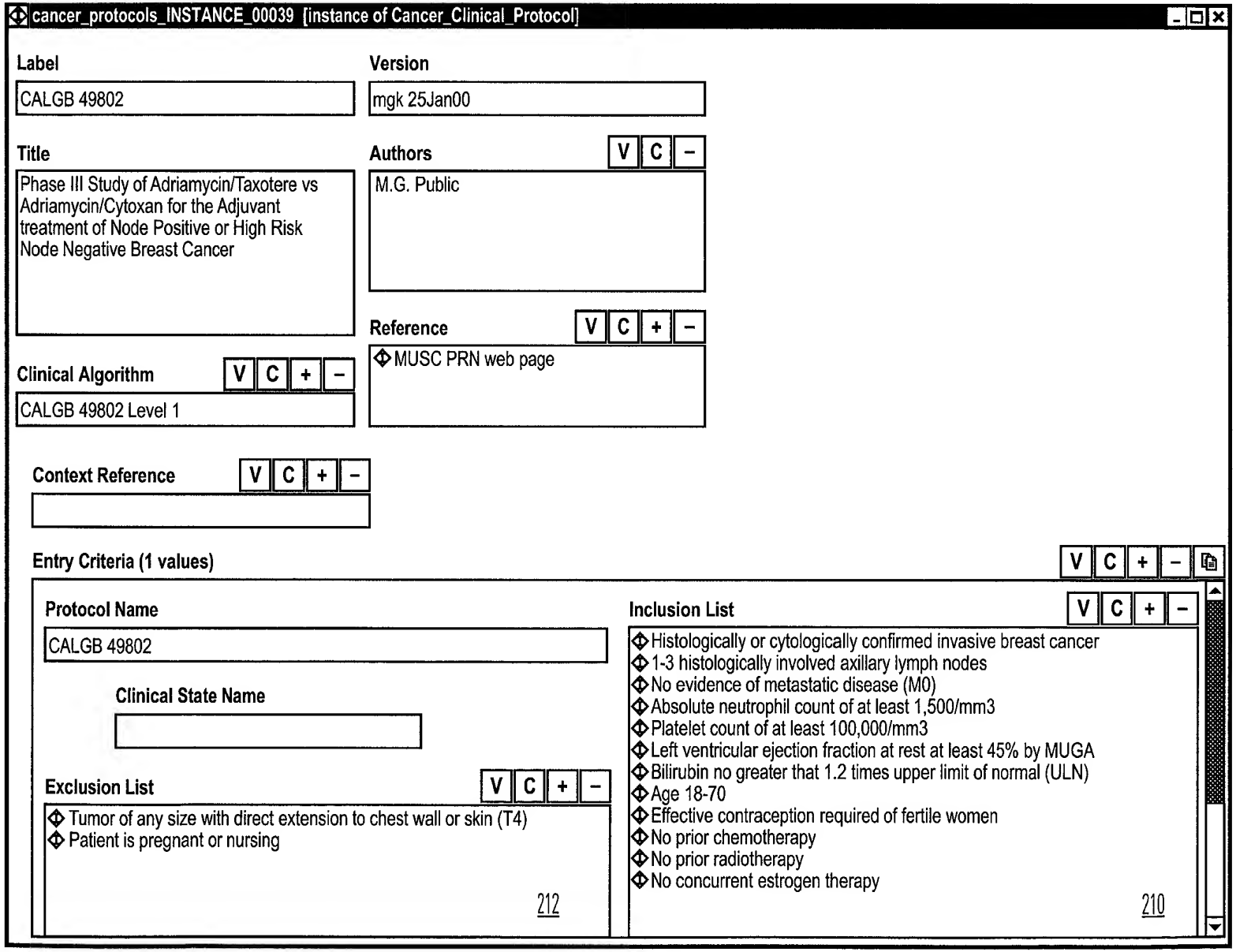


FIG. 2

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

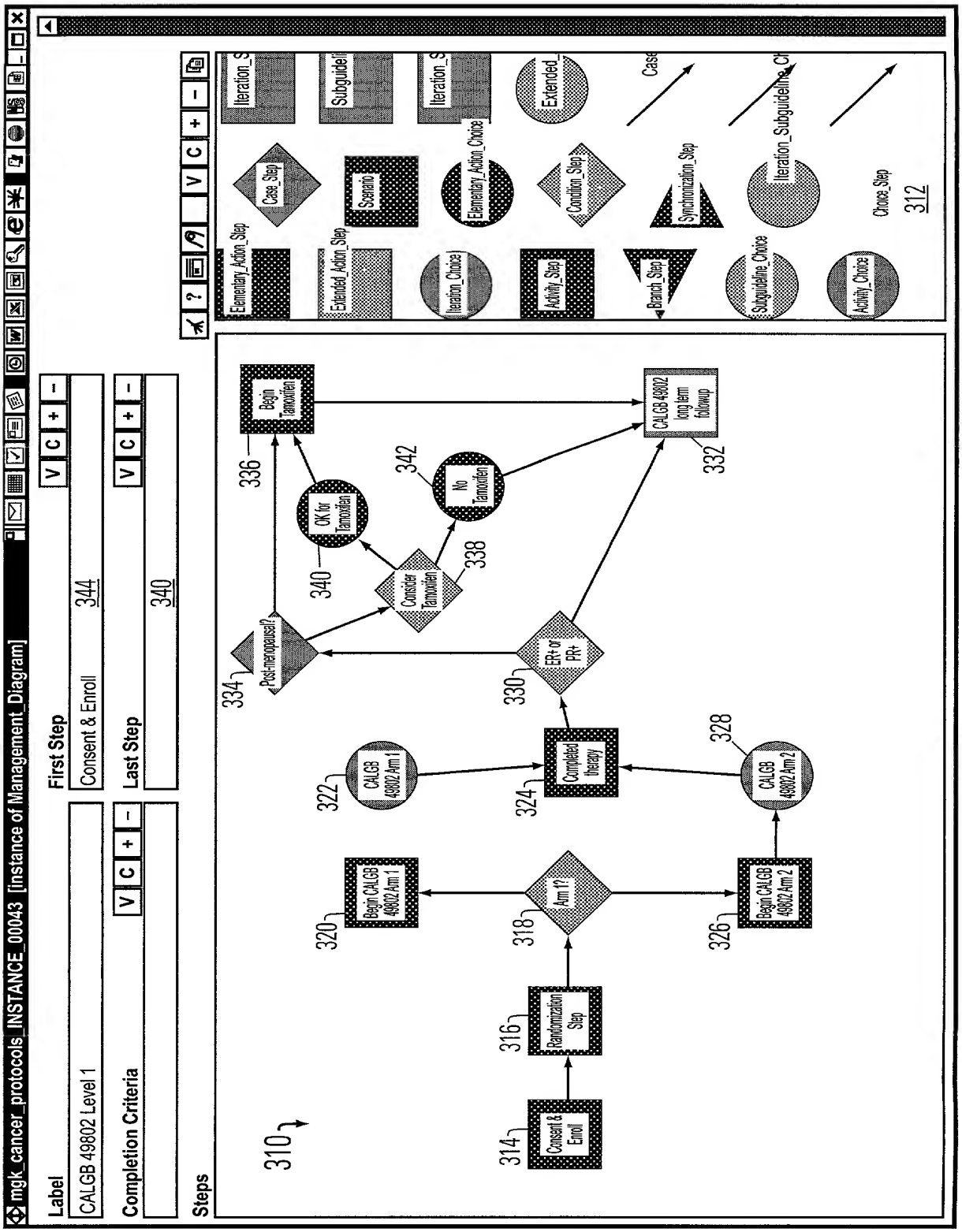

mgk_cancer_protocols_INSTANCE_00043 [instance of Management_Diagram]
Label
CALGB 49802 Level 1
Completion Criteria
First Step
Consent & Enroll
344
Last Step
340
Steps
310
Consent & Enroll
314
Randomization Step
316
Arm 1?
318
Begin CALGB 49802 Arm 1
320
CALGB 49802 Arm 1
322
Completed therapy
324
Begin CALGB 49802 Arm 2
326
CALGB 49802 Arm 2
328
ER+ or PR+
330
CALGB 49802 long term followup
332
Post-menopause!?
334
Consider Tamoxifen
338
OK for Tamoxifen
340
Begin Tamoxifen
336
No Tamoxifen
342
Elementary_Action_Step
Extended_Action_Step
Iteration_Choice
Case_Step
Scenario
Elementary_Action_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Subguideline_Choice
Iteration_Subguideline_Ch
Activity_Choice
Choice_Step
312

FIG. 3

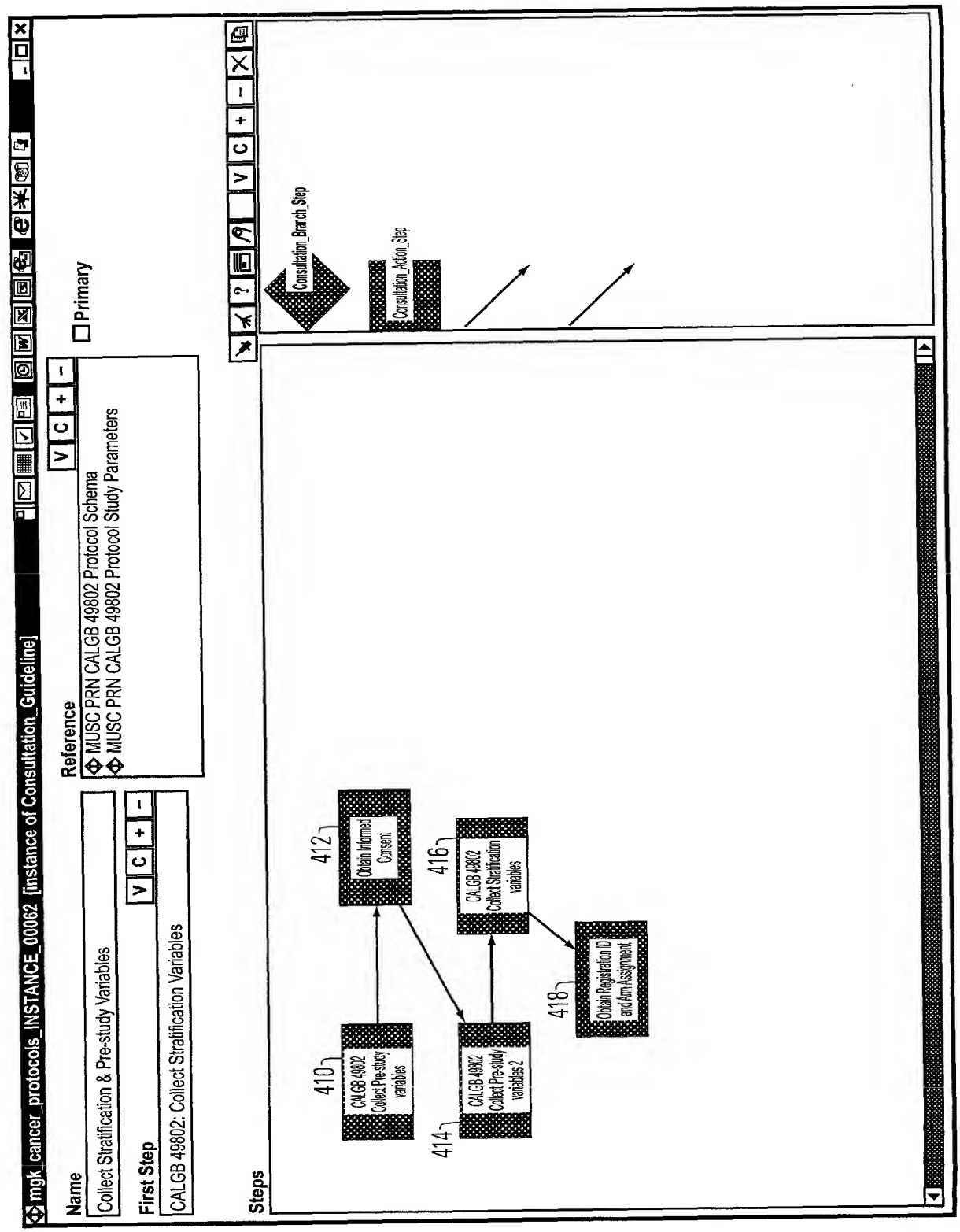

mgk_cancer_protocols_INSTANCE_00062 [instance of Consultation_Guideline]
Name
Collect Stratification & Pre-study Variables
First Step
CALGB 49802: Collect Stratification Variables
Reference
MUSC PRN CALGB 49802 Protocol Schema
MUSC PRN CALGB 49802 Protocol Study Parameters
Primary
Steps
Consultation_Branch_Step
Consultation_Action_Step
412
Obtain Informed Consent
410
CALGB 49802 Collect Pre-study variables
414
CALGB 49802 Collect Pre-study variables 2
416
CALGB 49802 Collect Stratification variables
418
Obtain Registration ID and Arm Assignment

FIG. 4

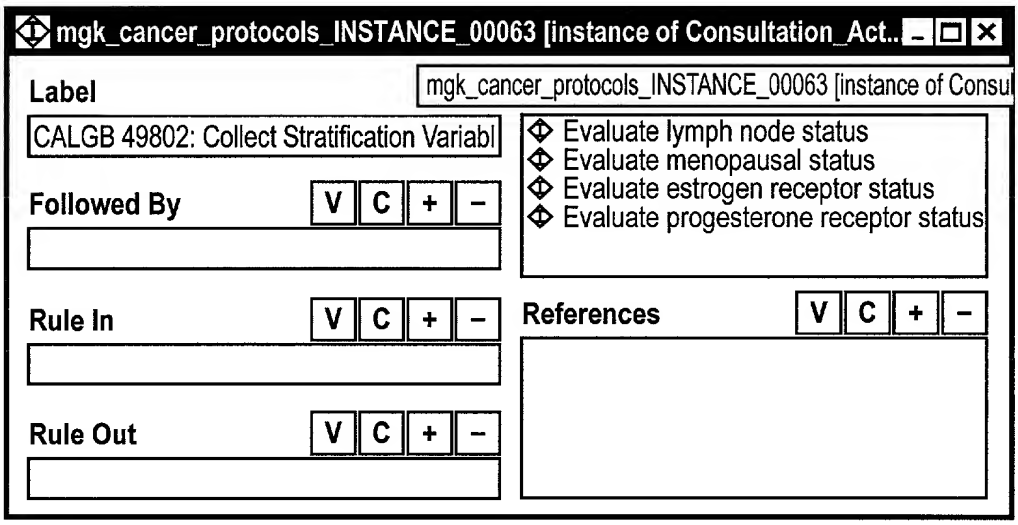

mgk_cancer_protocols_INSTANCE_00063 [instance of Consultation_Act..
Label
mgk_cancer_protocols_INSTANCE_00063 [instance of Consul
CALGB 49802: Collect Stratification Variabl
Evaluate lymph node status
Evaluate menopausal status
Evaluate estrogen receptor status
Evaluate progesterone receptor status
Followed By
V C + –
Rule In
V C + –
References
V C + –
Rule Out
V C + –

FIG. 5

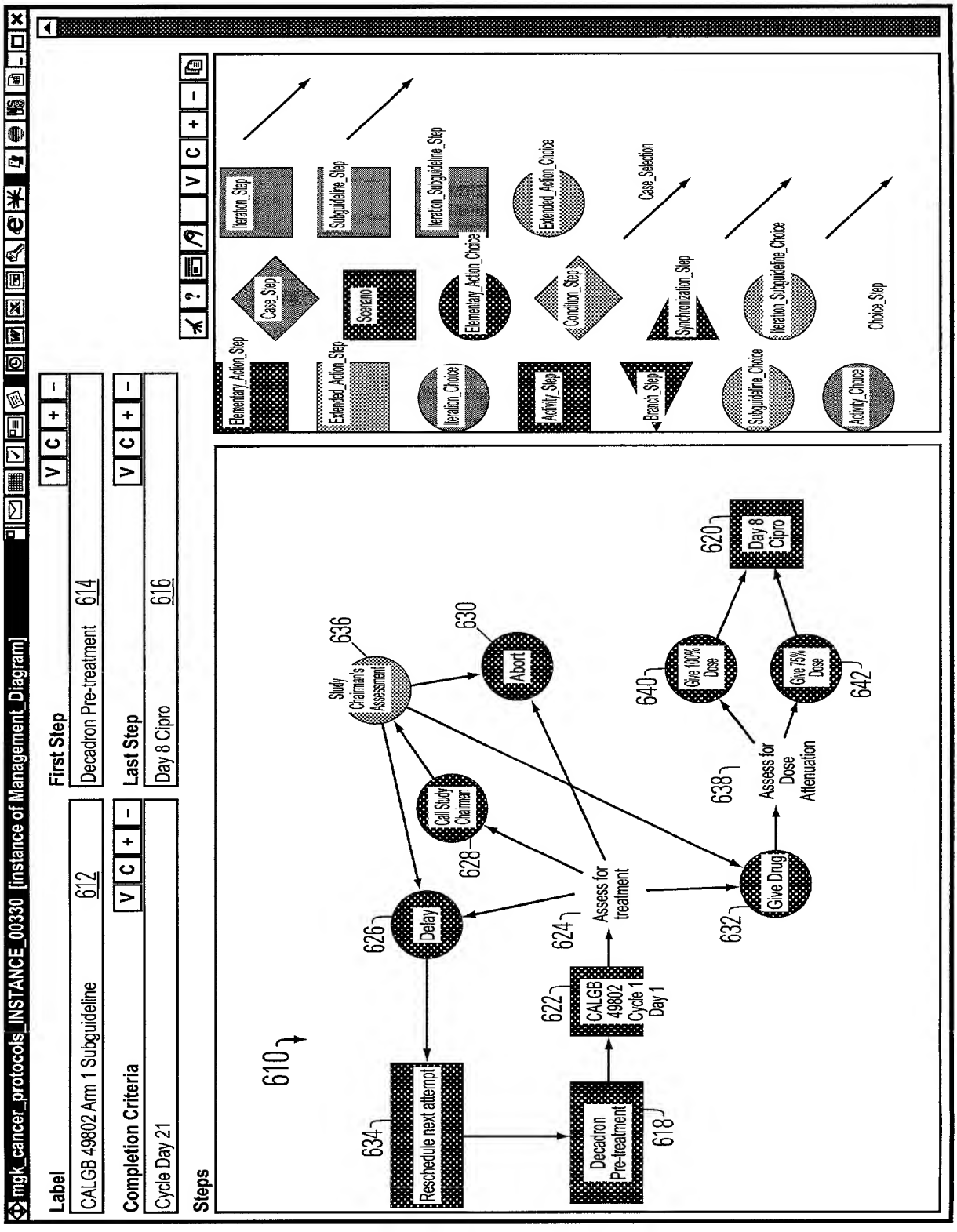

mgk_cancer_protocols_INSTANCE_00330 [instance of Management_Diagram]
Label
CALGB 49802 Arm 1 Subguideline
612
First Step
Decadron Pre-treatment
614
Completion Criteria
Cycle Day 21
Last Step
Day 8 Cipro
616
Steps
610
Elementary_Action_Step
Case_Step
Iteration_Step
Extended_Action_Step
Scenario
Subguideline_Step
Iteration_Choice
Elementary_Action_Choice
Iteration_Subguideline_Step
Activity_Step
Condition_Step
Extended_Action_Choice
Branch_Step
Synchronization_Step
Case_Selection
Subguideline_Choice
Iteration_Subguideline_Choice
Activity_Choice
Choice_Step
634
Reschedule next attempt
618
Decadron Pre-treatment
622
CALGB 49802 Cycle 1 Day 1
624
Assess for treatment
626
Delay
628
Call Study Chairman
636
Study Chairman's Assessment
630
Abort
632
Give Drug
638
Assess for Dose Attenuation
640
Give 100% Dose
642
Give 75% Dose
620
Day 8 Cipro

FIG. 6

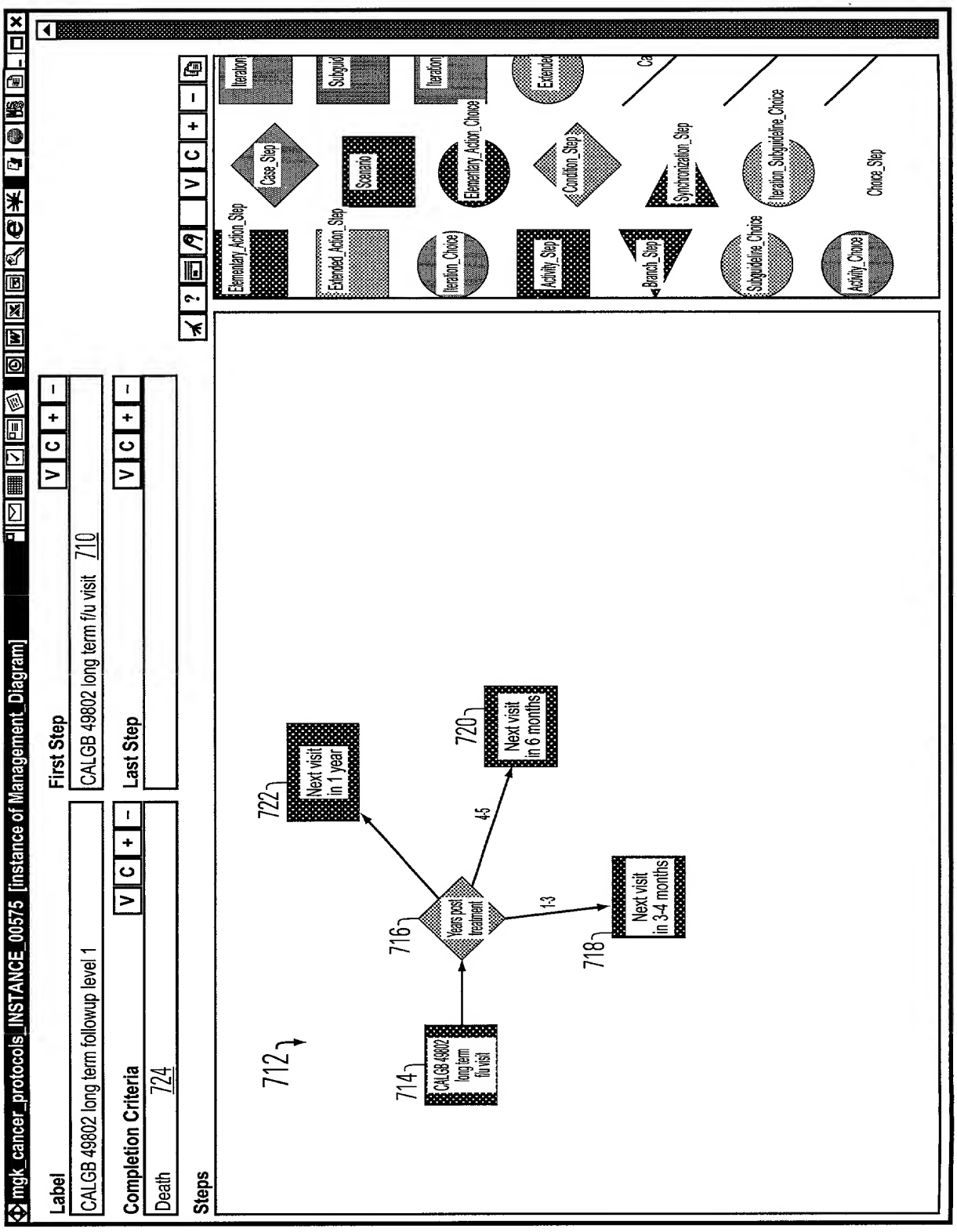

mgk_cancer_protocols_INSTANCE_00575 [instance of Management_Diagram]
Label
CALGB 49802 long term followup level 1
First Step
CALGB 49802 long term f/u visit 710
Completion Criteria
Death 724
Last Step
Steps
712
714
CALGB 49802 long term f/u visit
716
Years post treatment
718
Next visit in 3-4 months
720
Next visit in 6 months
722
Next visit in 1 year
1-3
4-5
Elementary_Action_Step
Extended_Action_Step
Iteration_Choice
Activity_Step
Branch_Step
Case_Step
Scenario
Elementary_Action_Choice
Condition_Step
Synchronization_Step
Subguideline_Choice
Activity_Choice
Iteration
Subguid
Extended
Iteration_Subguideline_Choice
Choice_Step

FIG. 7

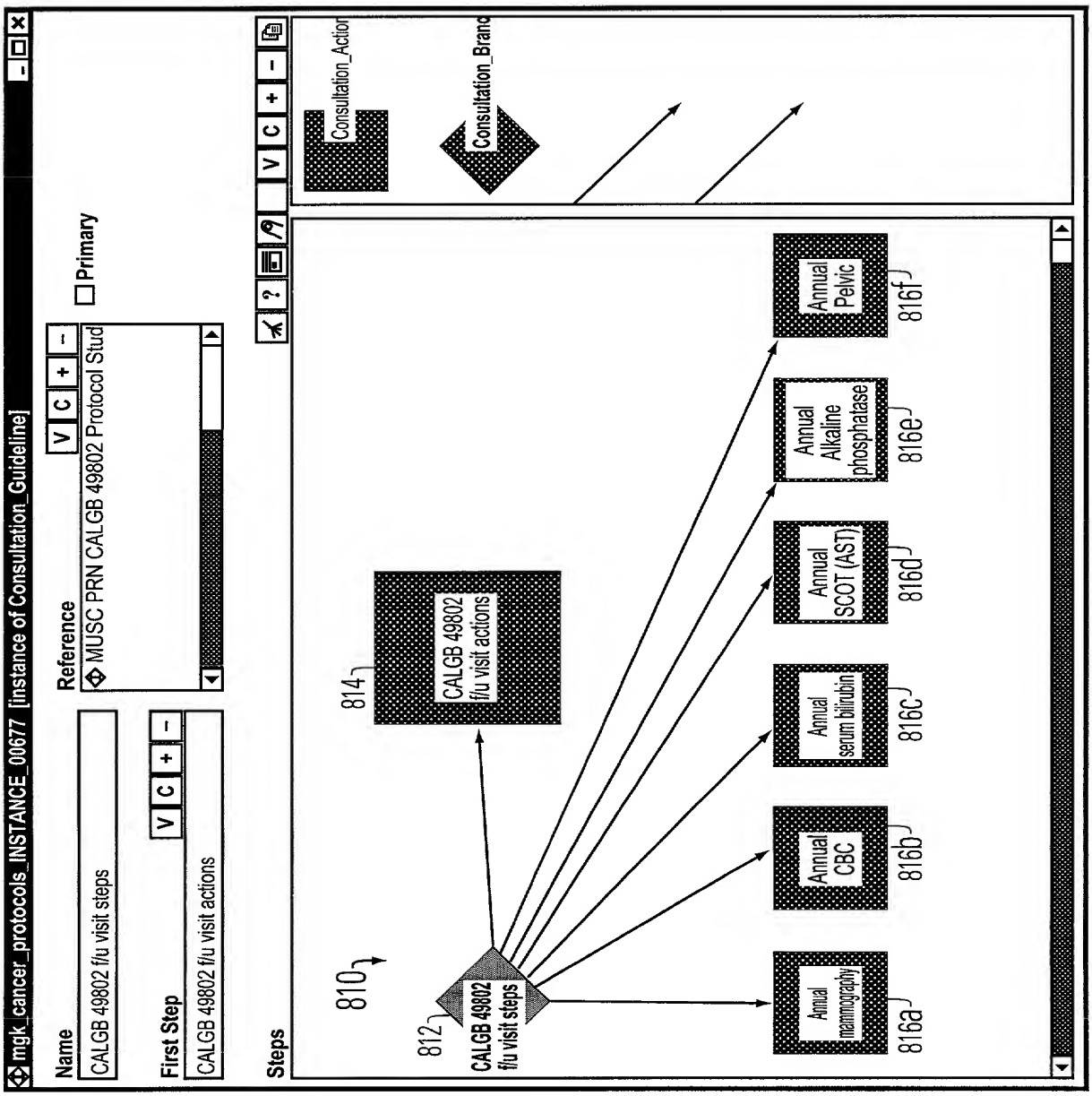

mgk_cancer_protocols_INSTANCE_00677 [instance of Consultation_Guideline]
Name
CALGB 49802 f/u visit steps
Reference
MUSC PRN CALGB 49802 Protocol Stud
Primary
First Step
CALGB 49802 f/u visit actions
Steps
810
812
CALGB 49802 f/u visit steps
814
CALGB 49802 f/u visit actions
Annual mammography
816a
Annual CBC
816b
Annual serum bilirubin
816c
Annual SCOT (AST)
816d
Annual Alkaline phosphatase
816e
Annual Pelvic
816f
Consultation_Action
Consultation_Brand

FIG. 8

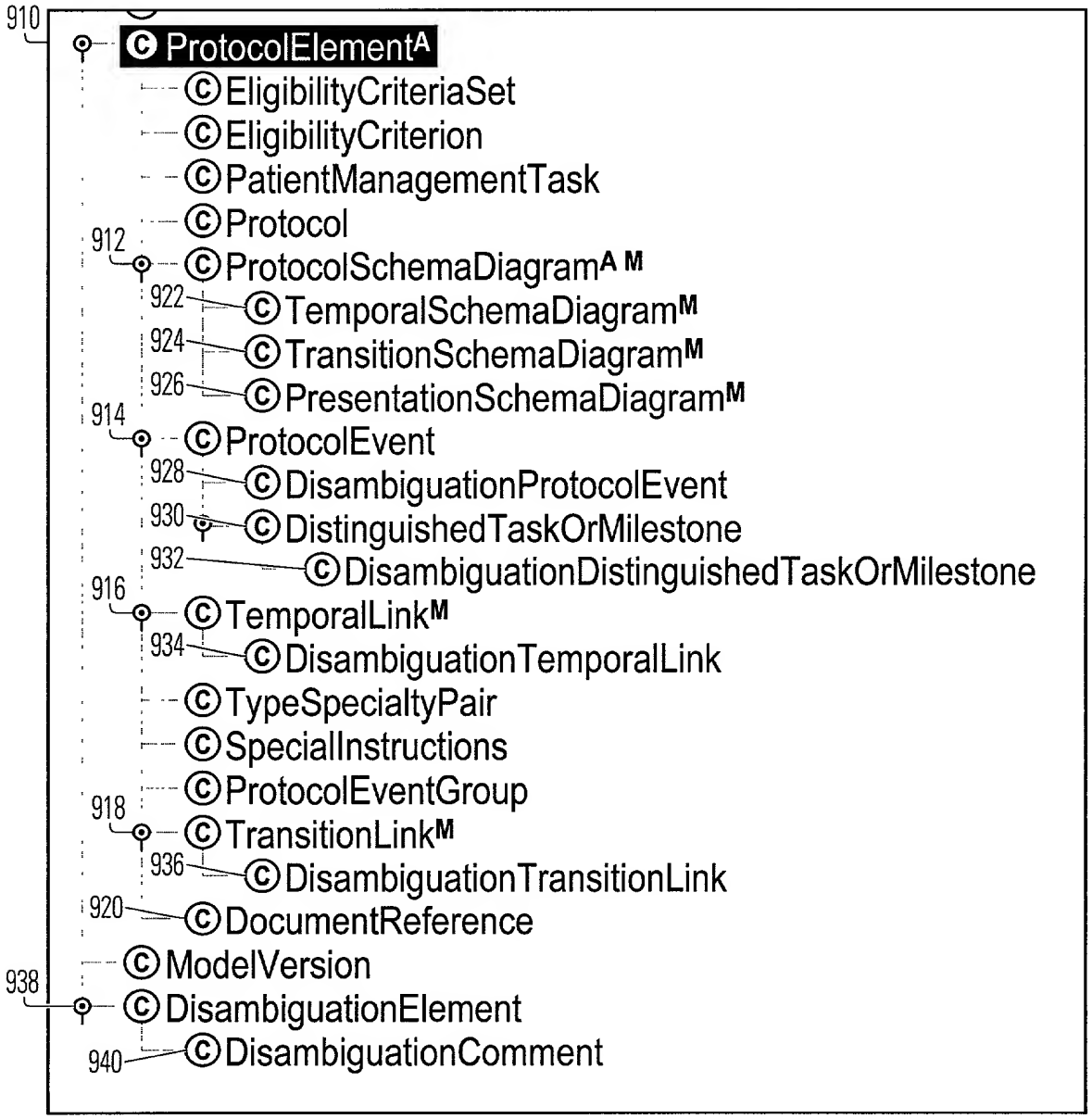


FIG. 9

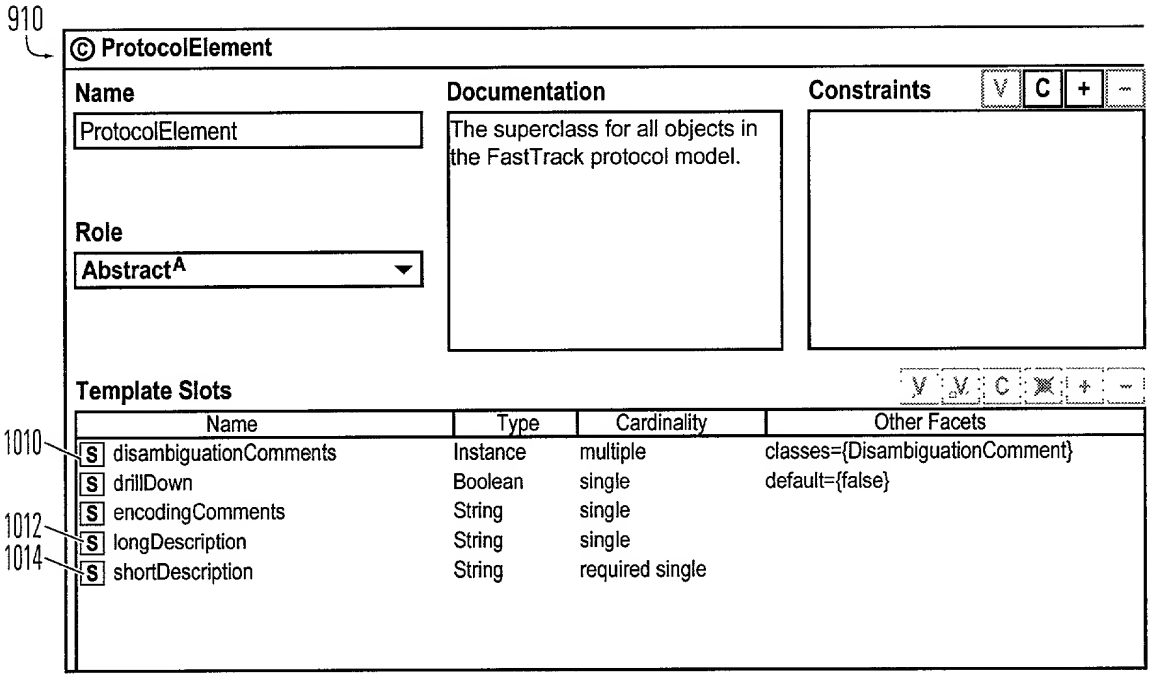

910
© ProtocolElement
Name
ProtocolElement
Documentation
The superclass for all objects in the FastTrack protocol model.
Constraints
V C + -
Role
Abstract^A
Template Slots
V V C + -
Name
Type
Cardinality
Other Facets
1010
S disambiguationComments
Instance
multiple
classes={DisambiguationComment}
S drillDown
Boolean
single
default={false}
S encodingComments
String
single
1012
S longDescription
String
single
1014
S shortDescription
String
required single

FIG. 10

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

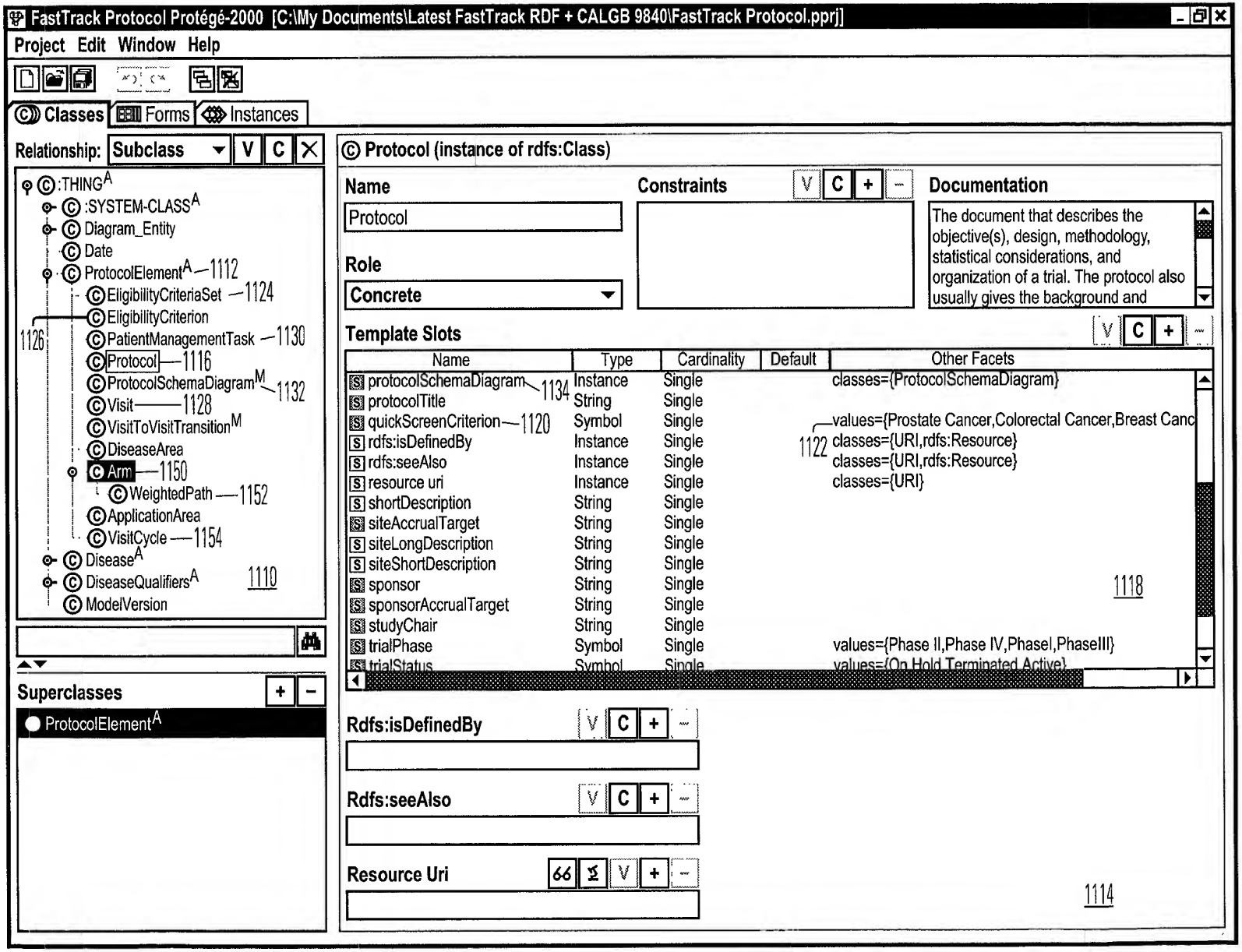


FIG. 11

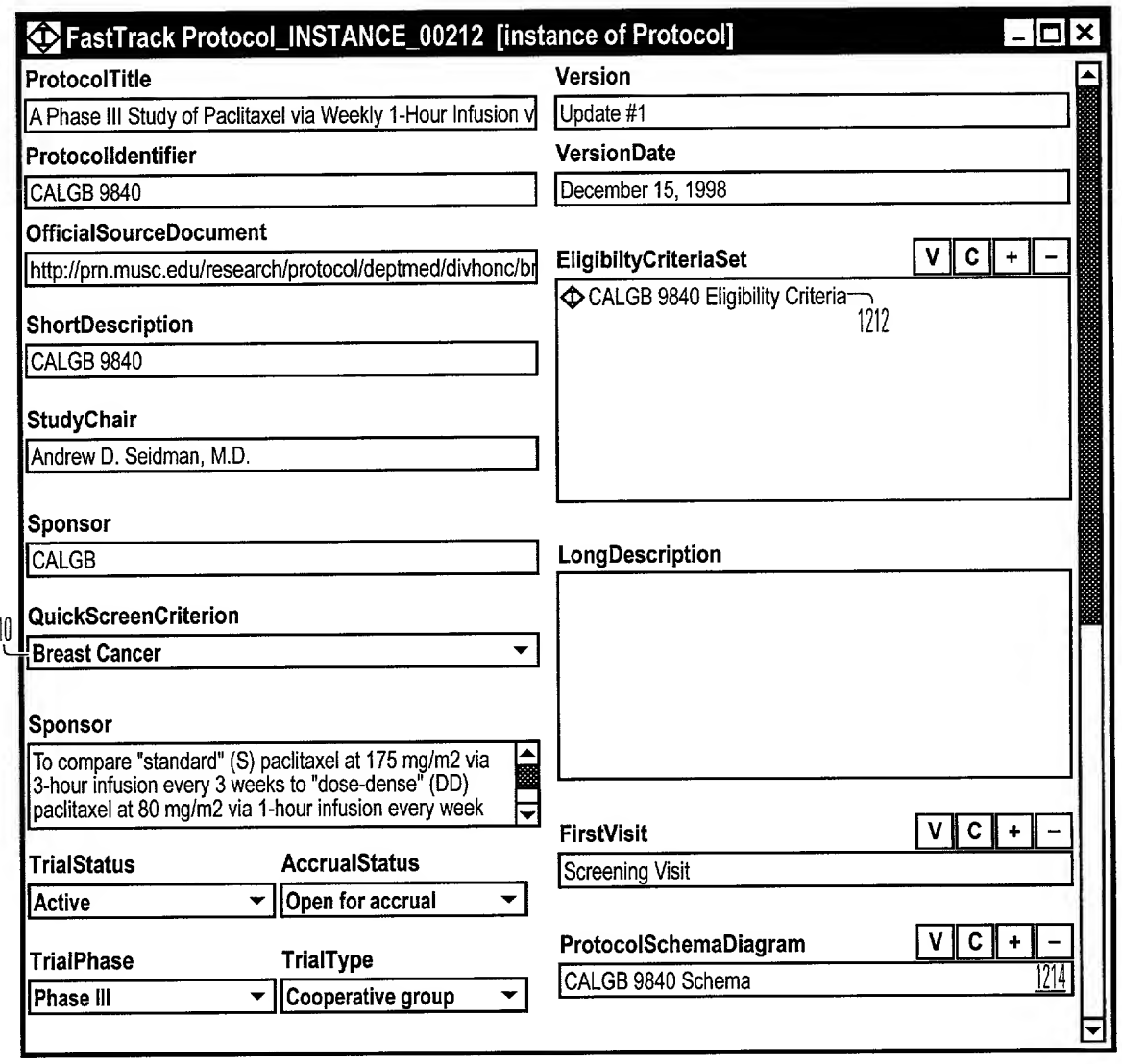

FastTrack Protocol_INSTANCE_00212 [instance of Protocol]
ProtocolTitle
A Phase III Study of Paclitaxel via Weekly 1-Hour Infusion v
Version
Update #1
ProtocolIdentifier
CALGB 9840
VersionDate
December 15, 1998
OfficialSourceDocument
http://prn.musc.edu/research/protocol/deptmed/divhonc/br
EligibiltyCriteriaSet
V C + -
CALGB 9840 Eligibility Criteria
1212
ShortDescription
CALGB 9840
StudyChair
Andrew D. Seidman, M.D.
Sponsor
CALGB
LongDescription
1210
QuickScreenCriterion
Breast Cancer
Sponsor
To compare "standard" (S) paclitaxel at 175 mg/m2 via 3-hour infusion every 3 weeks to "dose-dense" (DD) paclitaxel at 80 mg/m2 via 1-hour infusion every week
FirstVisit
V C + -
Screening Visit
TrialStatus
Active
AccrualStatus
Open for accrual
ProtocolSchemaDiagram
V C + -
CALGB 9840 Schema
1214
TrialPhase
Phase III
TrialType
Cooperative group

FIG. 12

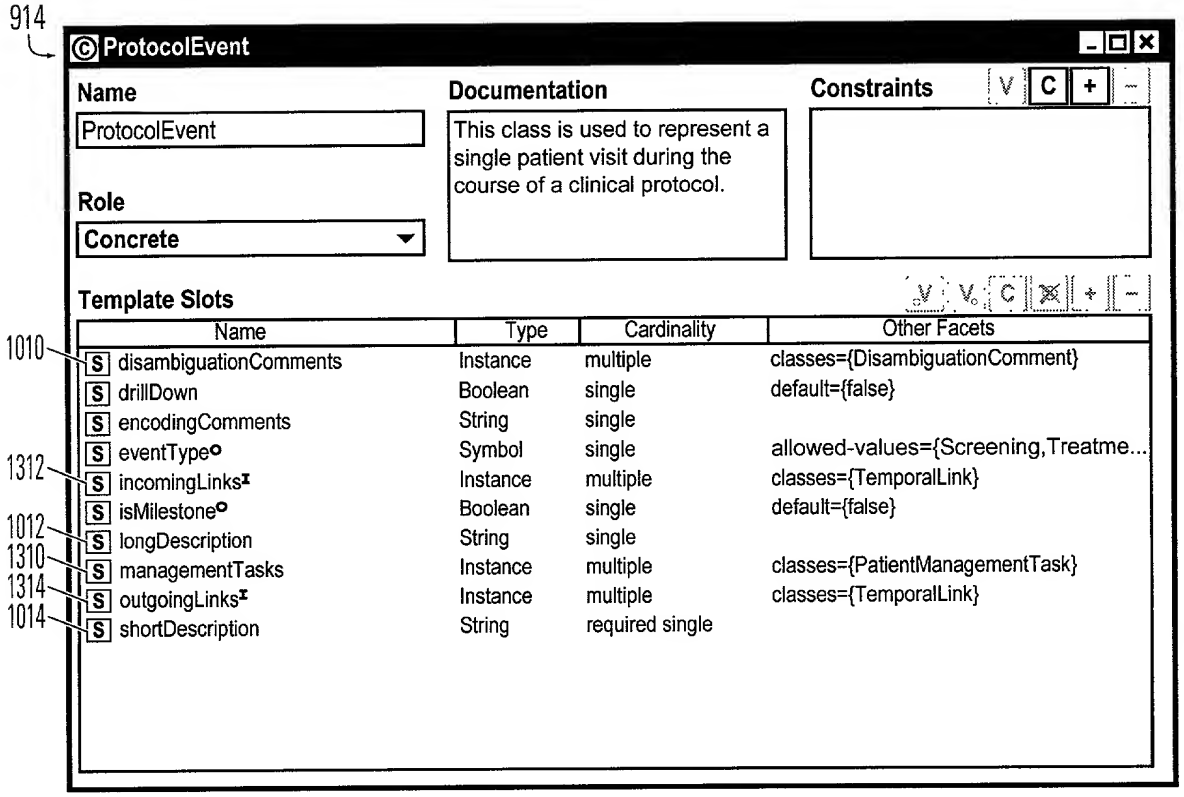

914
ProtocolEvent
Name
ProtocolEvent
Documentation
This class is used to represent a single patient visit during the course of a clinical protocol.
Constraints
Role
Concrete
Template Slots
Name
Type
Cardinality
Other Facets
1010
disambiguationComments
Instance
multiple
classes={DisambiguationComment}
drillDown
Boolean
single
default={false}
encodingComments
String
single
eventType
Symbol
single
allowed-values={Screening,Treatme...
1312
incomingLinks
Instance
multiple
classes={TemporalLink}
isMilestone
Boolean
single
default={false}
1012
longDescription
String
single
1310
managementTasks
Instance
multiple
classes={PatientManagementTask}
1314
outgoingLinks
Instance
multiple
classes={TemporalLink}
1014
shortDescription
String
required single

FIG. 13

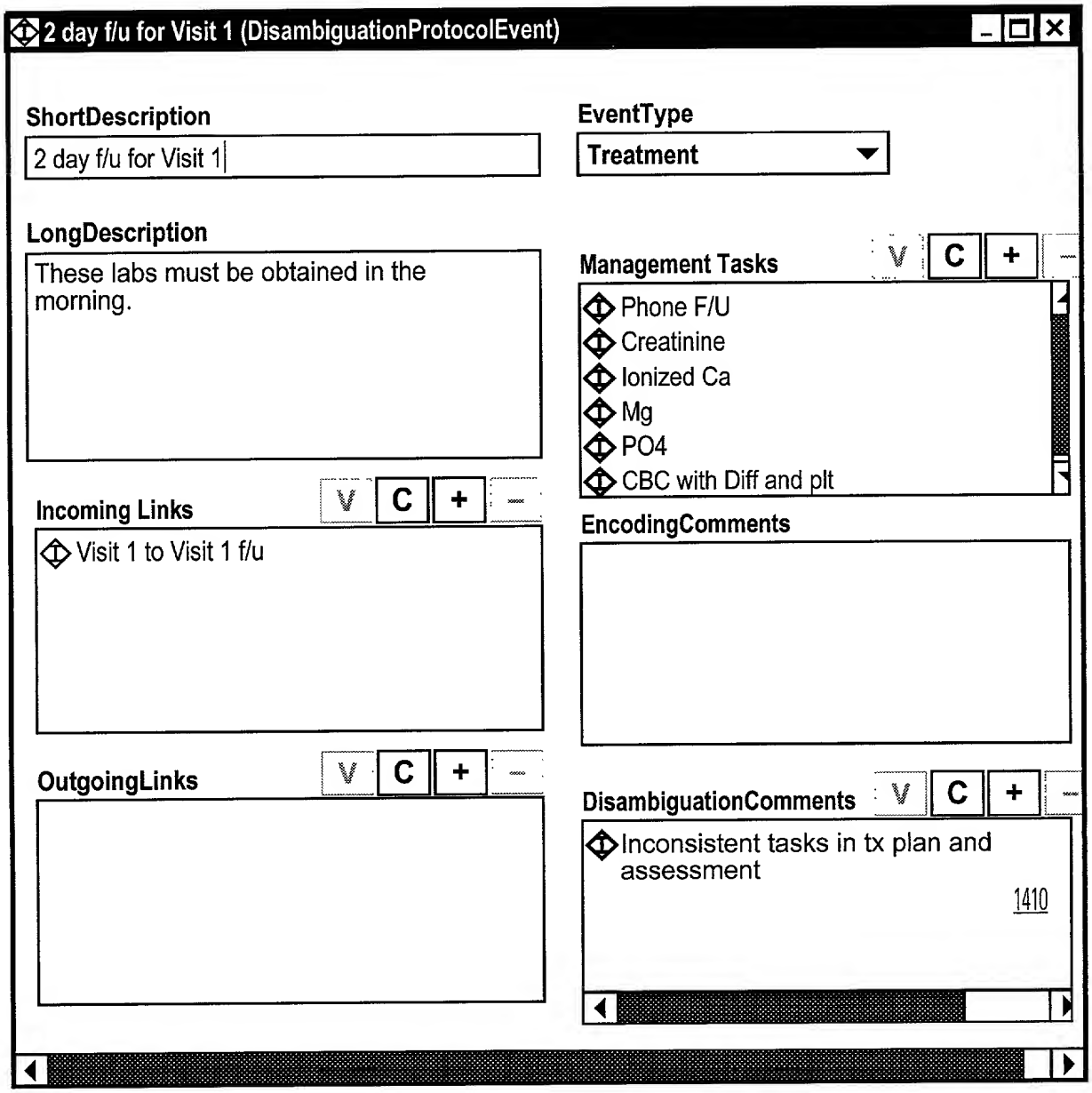
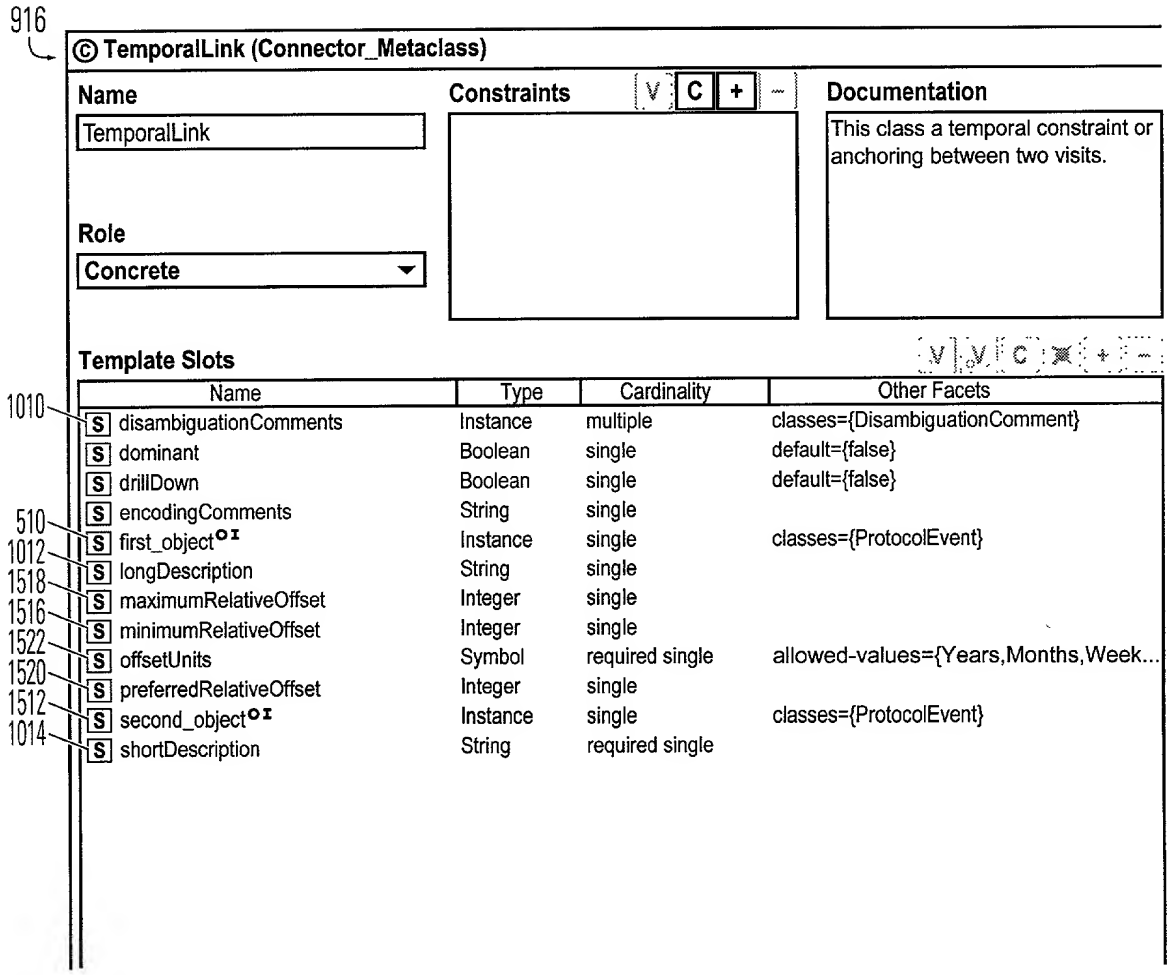

2 day f/u for Visit 1 (DisambiguationProtocolEvent)
ShortDescription
2 day f/u for Visit 1
EventType
Treatment
LongDescription
These labs must be obtained in the morning.
Management Tasks
V
C
+
Phone F/U
Creatinine
Ionized Ca
Mg
PO4
CBC with Diff and plt
Incoming Links
Visit 1 to Visit 1 f/u
EncodingComments
OutgoingLinks
DisambiguationComments
Inconsistent tasks in tx plan and assessment
1410

FIG. 14



Name	Type	Cardinality	Other Facets
disambiguationComments	Instance	multiple	classes={DisambiguationComment}
dominant	Boolean	single	default={false}
drillDown	Boolean	single	default={false}
encodingComments	String	single	
first_object	Instance	single	classes={ProtocolEvent}
longDescription	String	single	
maximumRelativeOffset	Integer	single	
minimumRelativeOffset	Integer	single	
offsetUnits	Symbol	required single	allowed-values={Years,Months,Week...
preferredRelativeOffset	Integer	single	
second_object	Instance	single	classes={ProtocolEvent}
shortDescription	String	required single	

FIG. 15

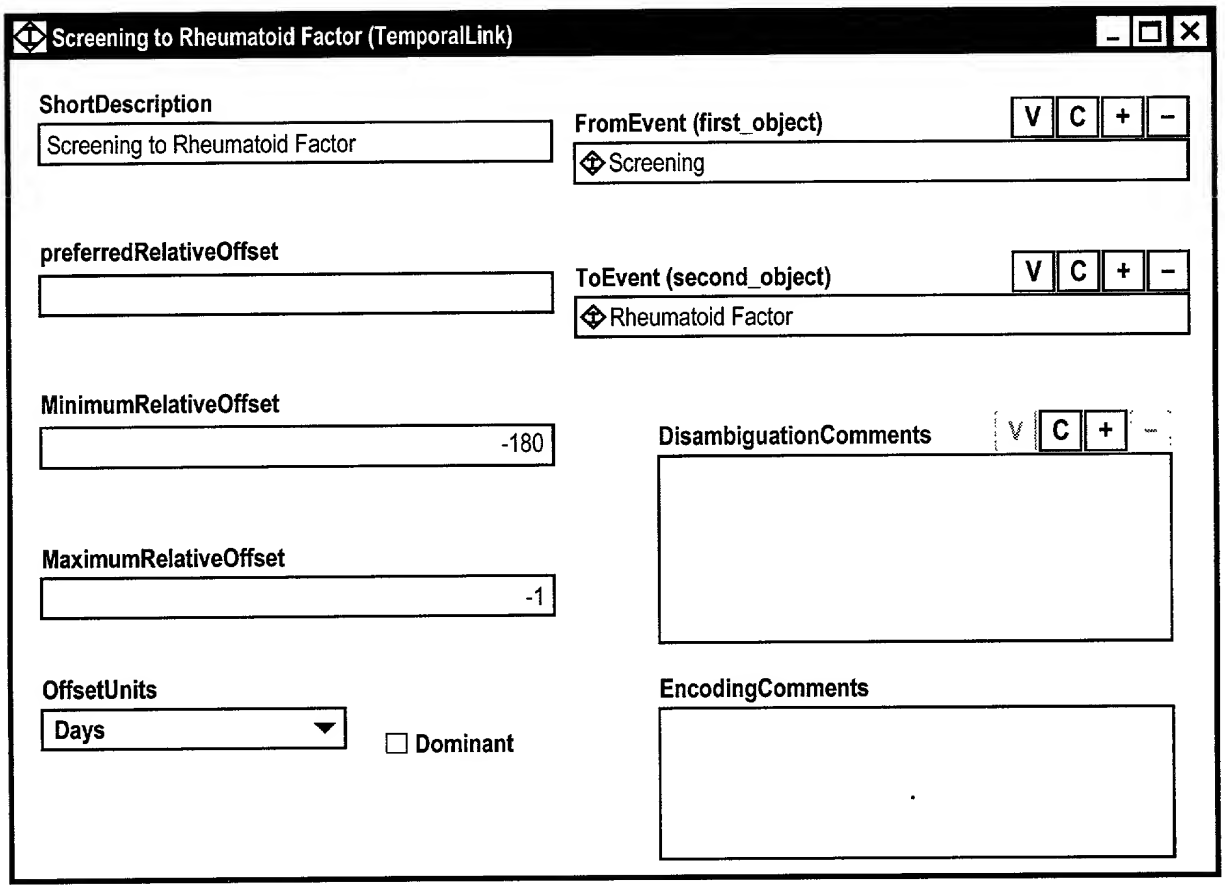

Screening to Rheumatoid Factor (TemporalLink)
ShortDescription
Screening to Rheumatoid Factor
FromEvent (first_object)
V C + -
Screening
preferredRelativeOffset
ToEvent (second_object)
V C + -
Rheumatoid Factor
MinimumRelativeOffset
-180
DisambiguationComments
V C + -
MaximumRelativeOffset
-1
OffsetUnits
Days
Dominant
EncodingComments

FIG. 16

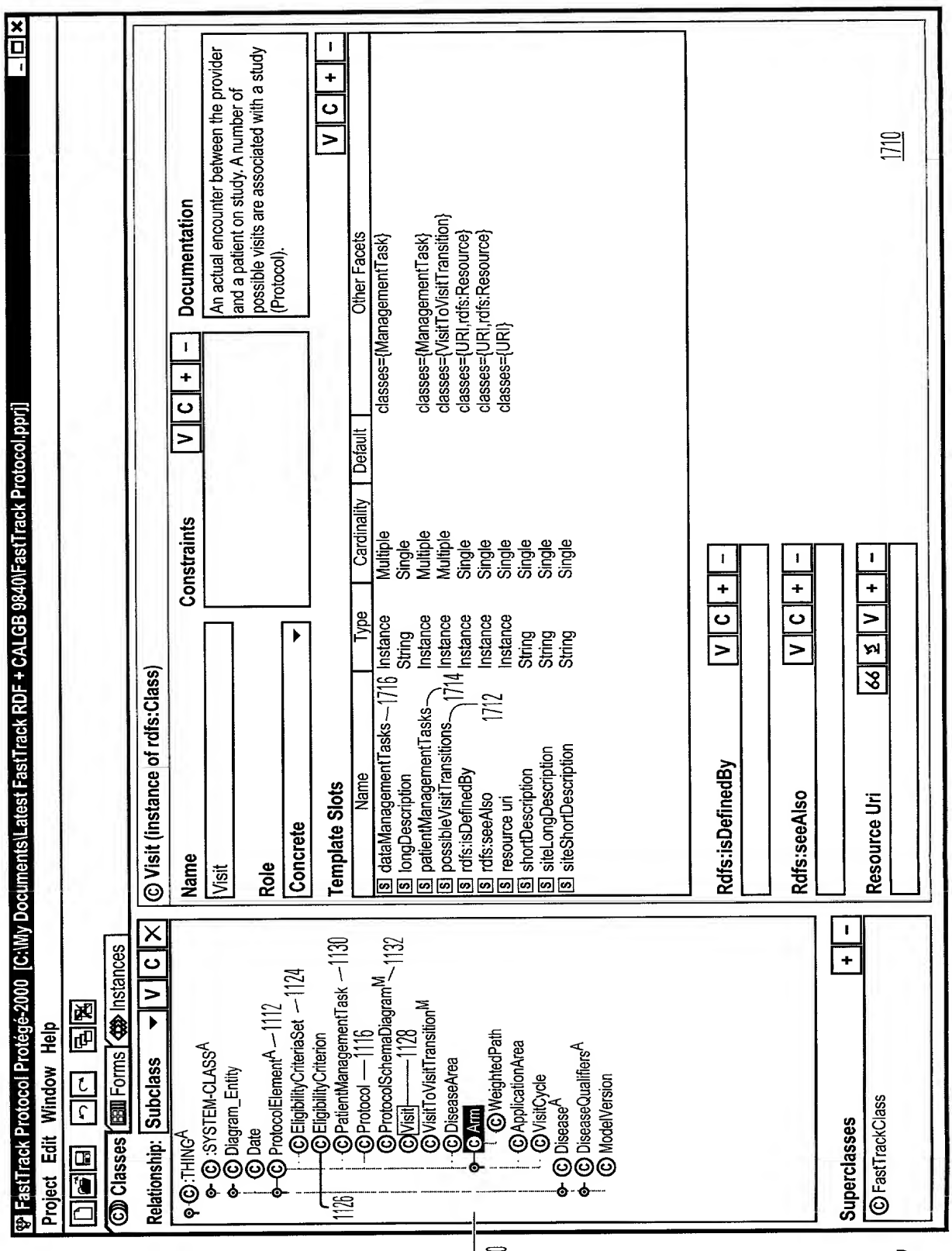

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass
:THING
:SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease
DiseaseQualifiers
ModelVersion
1110
1126
1112
1124
1130
1116
1132
1128
Superclasses
FastTrackClass
Visit (instance of rdfs:Class)
Name
Visit
Role
Concrete
Constraints
Documentation
An actual encounter between the provider and a patient on study. A number of possible visits are associated with a study (Protocol).
Template Slots
Name
Type
Cardinality
Default
Other Facets
dataManagementTasks
longDescription
patientManagementTasks
possibleVisitTransitions
rdfs:isDefinedBy
rdfs:seeAlso
resource uri
shortDescription
siteLongDescription
siteShortDescription
Instance
String
Instance
Instance
Instance
Instance
Instance
String
String
String
Multiple
Single
Multiple
Multiple
Single
Single
Single
Single
Single
Single
classes={ManagementTask}
classes={ManagementTask}
classes={VisitToVisitTransition}
classes={URI,rdfs:Resource}
classes={URI,rdfs:Resource}
classes={URI}
1716
1714
1712
Rdfs:isDefinedBy
Rdfs:seeAlso
Resource Uri
1710

FIG. 17

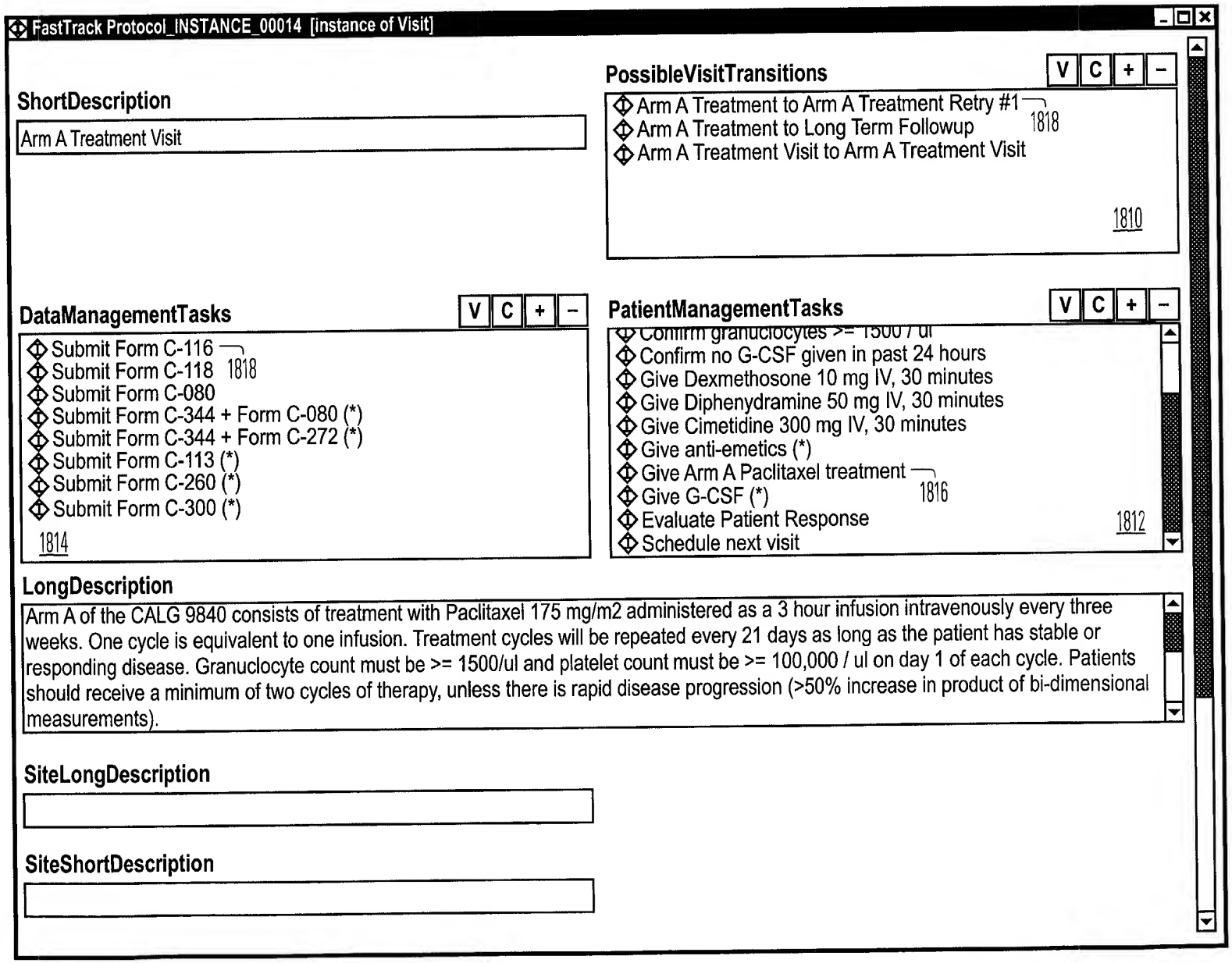

FastTrack Protocol_INSTANCE_00014 [instance of Visit]
ShortDescription
Arm A Treatment Visit
PossibleVisitTransitions
V C + −
Arm A Treatment to Arm A Treatment Retry #1
Arm A Treatment to Long Term Followup
Arm A Treatment Visit to Arm A Treatment Visit
1818
1810
DataManagementTasks
V C + −
Submit Form C-116
Submit Form C-118
Submit Form C-080
Submit Form C-344 + Form C-080 (*)
Submit Form C-344 + Form C-272 (*)
Submit Form C-113 (*)
Submit Form C-260 (*)
Submit Form C-300 (*)
1818
1814
PatientManagementTasks
V C + −
Confirm granulocytes >= 1500 / ul
Confirm no G-CSF given in past 24 hours
Give Dexmethosone 10 mg IV, 30 minutes
Give Diphenydramine 50 mg IV, 30 minutes
Give Cimetidine 300 mg IV, 30 minutes
Give anti-emetics (*)
Give Arm A Paclitaxel treatment
Give G-CSF (*)
Evaluate Patient Response
Schedule next visit
1816
1812
LongDescription
Arm A of the CALG 9840 consists of treatment with Paclitaxel 175 mg/m2 administered as a 3 hour infusion intravenously every three weeks. One cycle is equivalent to one infusion. Treatment cycles will be repeated every 21 days as long as the patient has stable or responding disease. Granuclocyte count must be >= 1500/ul and platelet count must be >= 100,000 / ul on day 1 of each cycle. Patients should receive a minimum of two cycles of therapy, unless there is rapid disease progression (>50% increase in product of bi-dimensional measurements).
SiteLongDescription
SiteShortDescription

FIG. 18

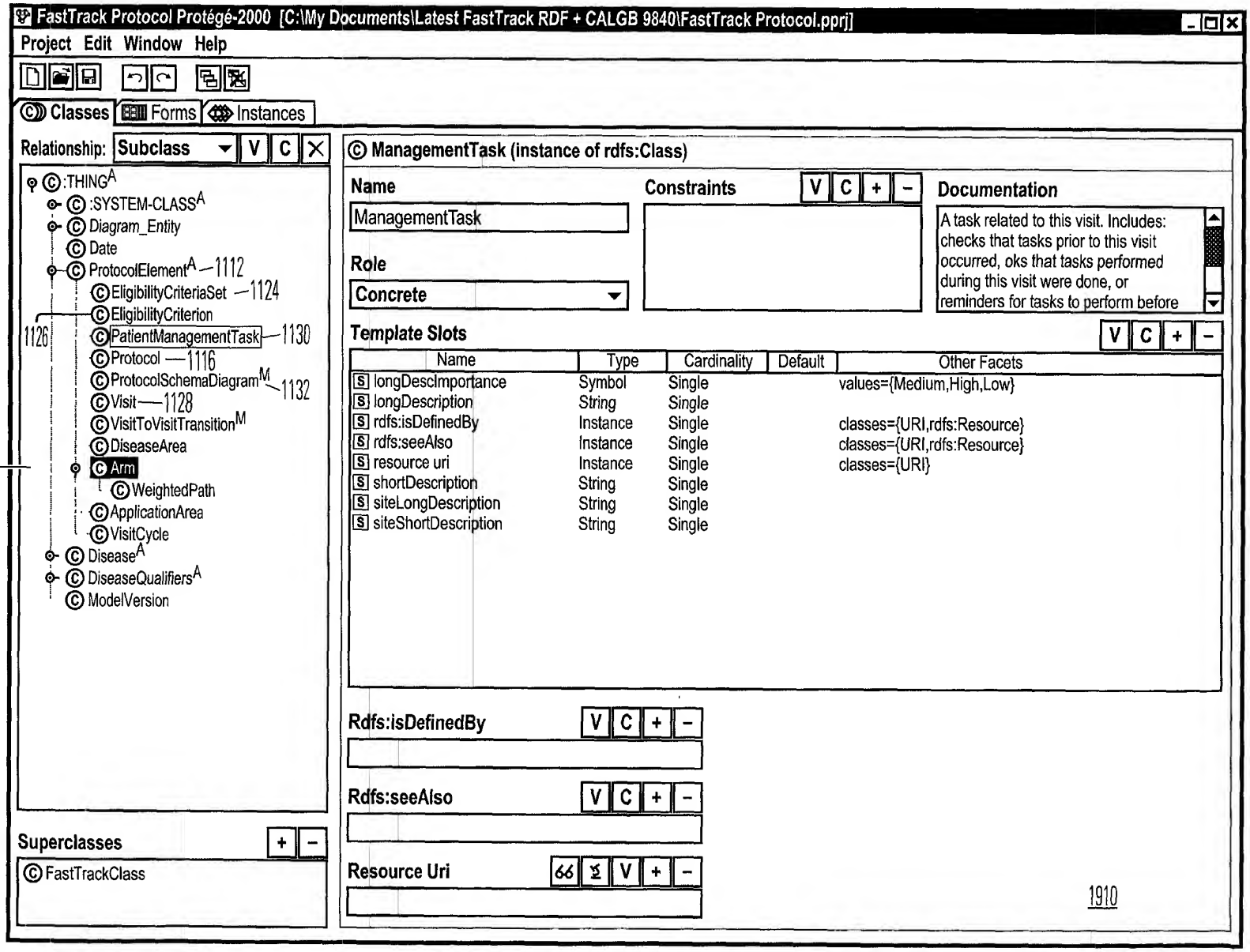

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass V C
:THING
:SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease
DiseaseQualifiers
ModelVersion
1112
1124
1126
1130
1116
1132
1128
1110
Superclasses
FastTrackClass
ManagementTask (instance of rdfs:Class)
Name
ManagementTask
Role
Concrete
Constraints
Documentation
A task related to this visit. Includes: checks that tasks prior to this visit occurred, oks that tasks performed during this visit were done, or reminders for tasks to perform before
Template Slots
Name | Type | Cardinality | Default | Other Facets
longDescImportance | Symbol | Single | values={Medium,High,Low}
longDescription | String | Single
rdfs:isDefinedBy | Instance | Single | classes={URI,rdfs:Resource}
rdfs:seeAlso | Instance | Single | classes={URI,rdfs:Resource}
resource uri | Instance | Single | classes={URI}
shortDescription | String | Single
siteLongDescription | String | Single
siteShortDescription | String | Single
Rdfs:isDefinedBy
Rdfs:seeAlso
Resource Uri
1910

FIG. 19

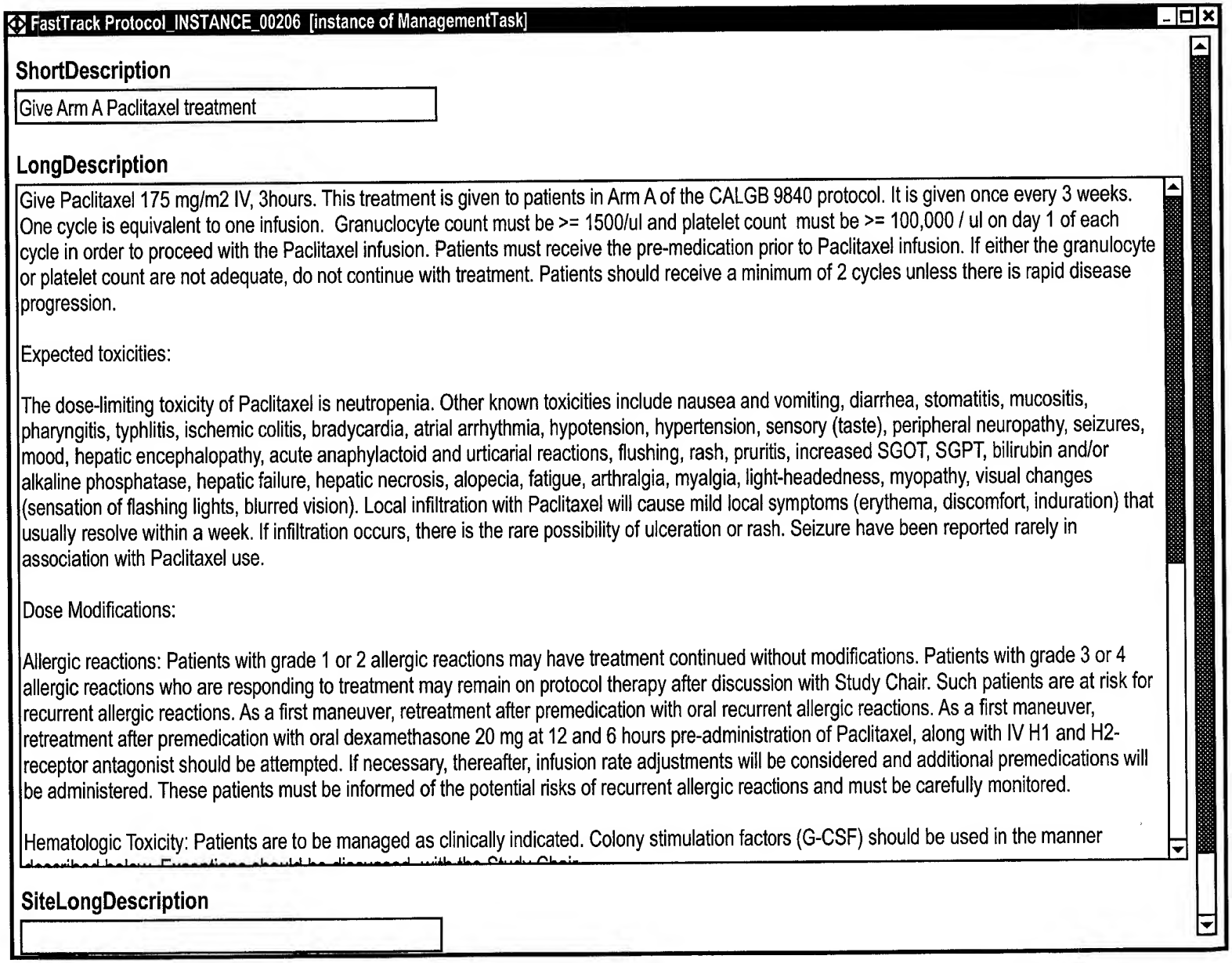


FIG. 20

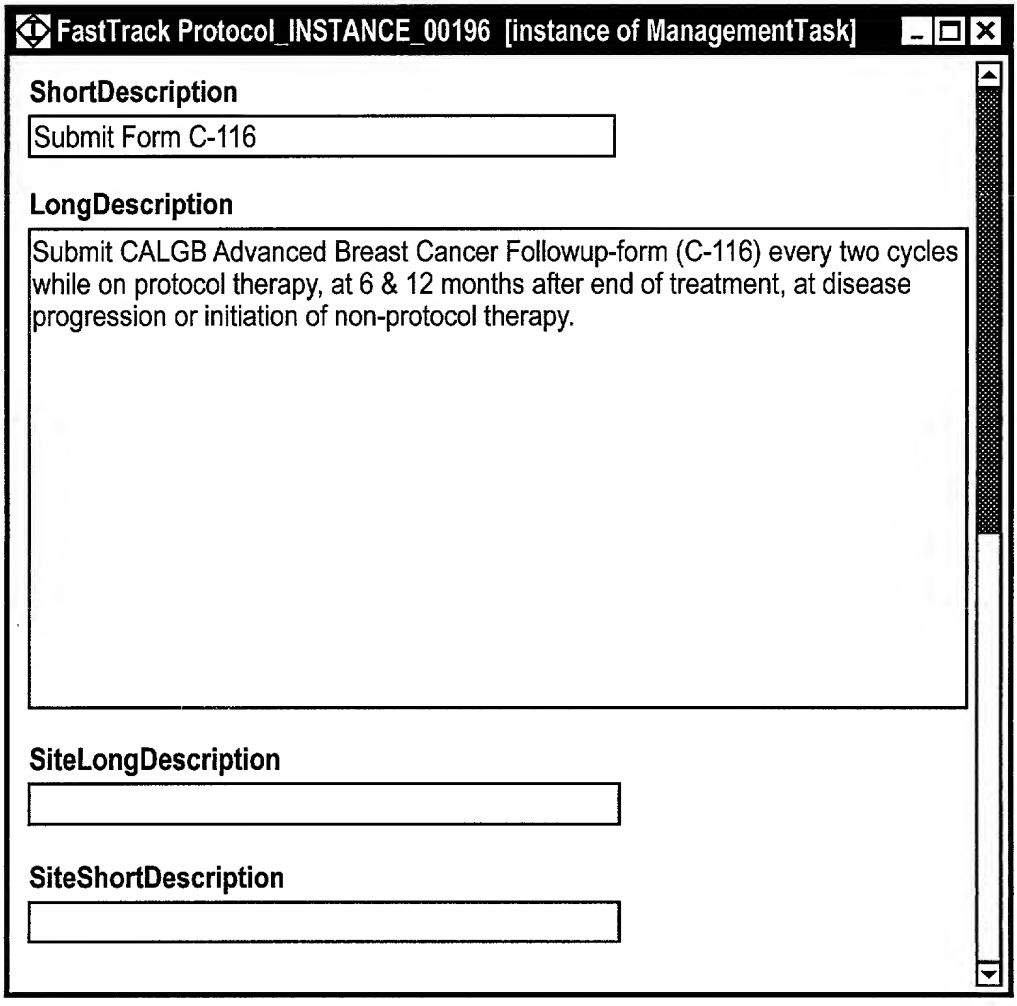

FastTrack Protocol_INSTANCE_00196 [instance of ManagementTask]
ShortDescription
Submit Form C-116
LongDescription
Submit CALGB Advanced Breast Cancer Followup-form (C-116) every two cycles while on protocol therapy, at 6 & 12 months after end of treatment, at disease progression or initiation of non-protocol therapy.
SiteLongDescription
SiteShortDescription

FIG. 21

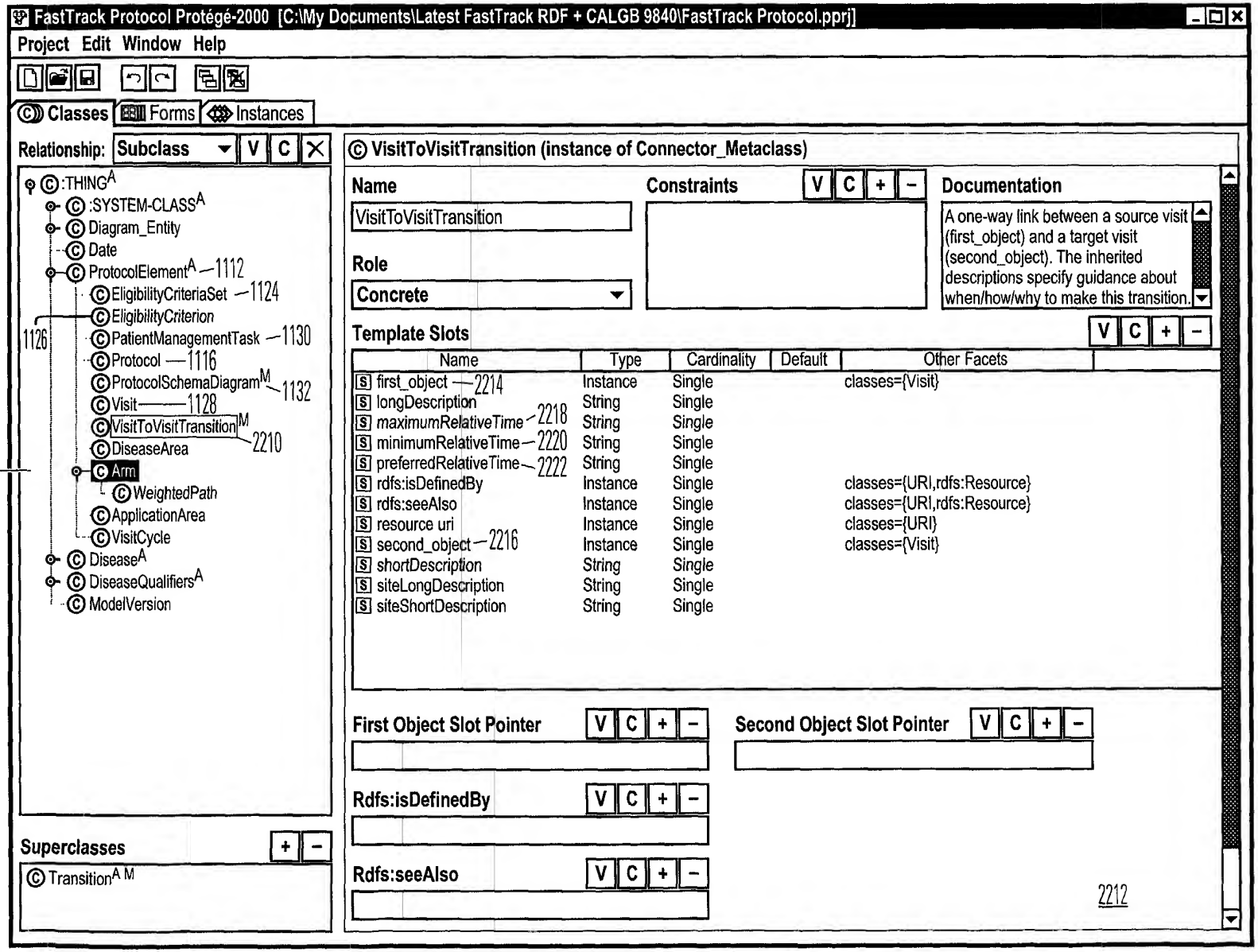

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass V C
:THING A
:SYSTEM-CLASS A
Diagram_Entity
Date
ProtocolElement A 1112
EligibilityCriteriaSet 1124
EligibilityCriterion
PatientManagementTask 1130
Protocol 1116
ProtocolSchemaDiagram M 1132
Visit 1128
VisitToVisitTransition M 2210
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease A
DiseaseQualifiers A
ModelVersion
1126
1110
Superclasses
Transition A M
VisitToVisitTransition (instance of Connector_Metaclass)
Name
VisitToVisitTransition
Constraints
Documentation
A one-way link between a source visit (first_object) and a target visit (second_object). The inherited descriptions specify guidance about when/how/why to make this transition.
Role
Concrete
Template Slots
Name | Type | Cardinality | Default | Other Facets
first_object 2214 | Instance | Single | | classes={Visit}
longDescription | String | Single
maximumRelativeTime 2218 | String | Single
minimumRelativeTime 2220 | String | Single
preferredRelativeTime 2222 | String | Single
rdfs:isDefinedBy | Instance | Single | | classes={URI,rdfs:Resource}
rdfs:seeAlso | Instance | Single | | classes={URI,rdfs:Resource}
resource uri | Instance | Single | | classes={URI}
second_object 2216 | Instance | Single | | classes={Visit}
shortDescription | String | Single
siteLongDescription | String | Single
siteShortDescription | String | Single
First Object Slot Pointer
Second Object Slot Pointer
Rdfs:isDefinedBy
Rdfs:seeAlso
2212

FIG. 22

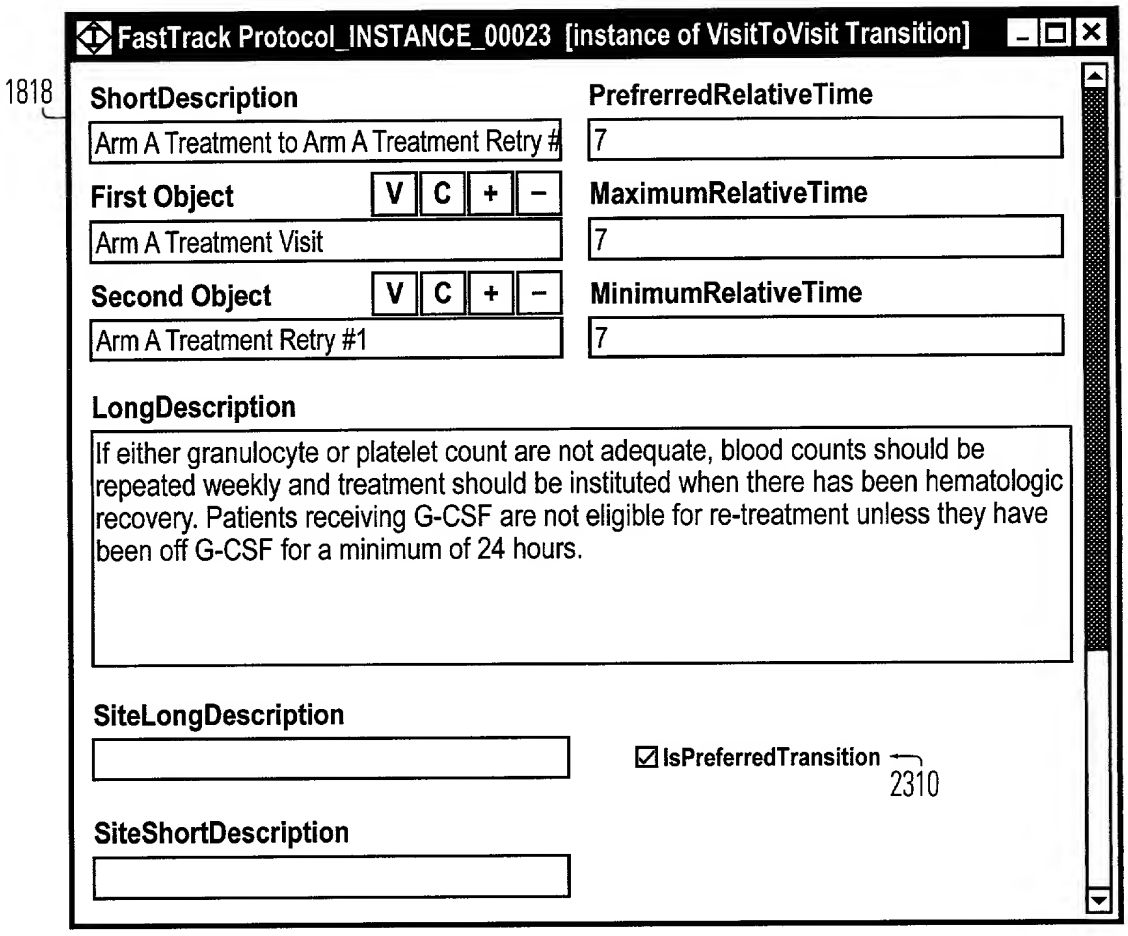

FastTrack Protocol_INSTANCE_00023 [instance of VisitToVisit Transition]
1818
ShortDescription
Arm A Treatment to Arm A Treatment Retry #
PrefrerredRelativeTime
7
First Object
V
C
+
−
Arm A Treatment Visit
MaximumRelativeTime
7
Second Object
V
C
+
−
Arm A Treatment Retry #1
MinimumRelativeTime
7
LongDescription
If either granulocyte or platelet count are not adequate, blood counts should be repeated weekly and treatment should be instituted when there has been hematologic recovery. Patients receiving G-CSF are not eligible for re-treatment unless they have been off G-CSF for a minimum of 24 hours.
SiteLongDescription
IsPreferredTransition
2310
SiteShortDescription

FIG. 23

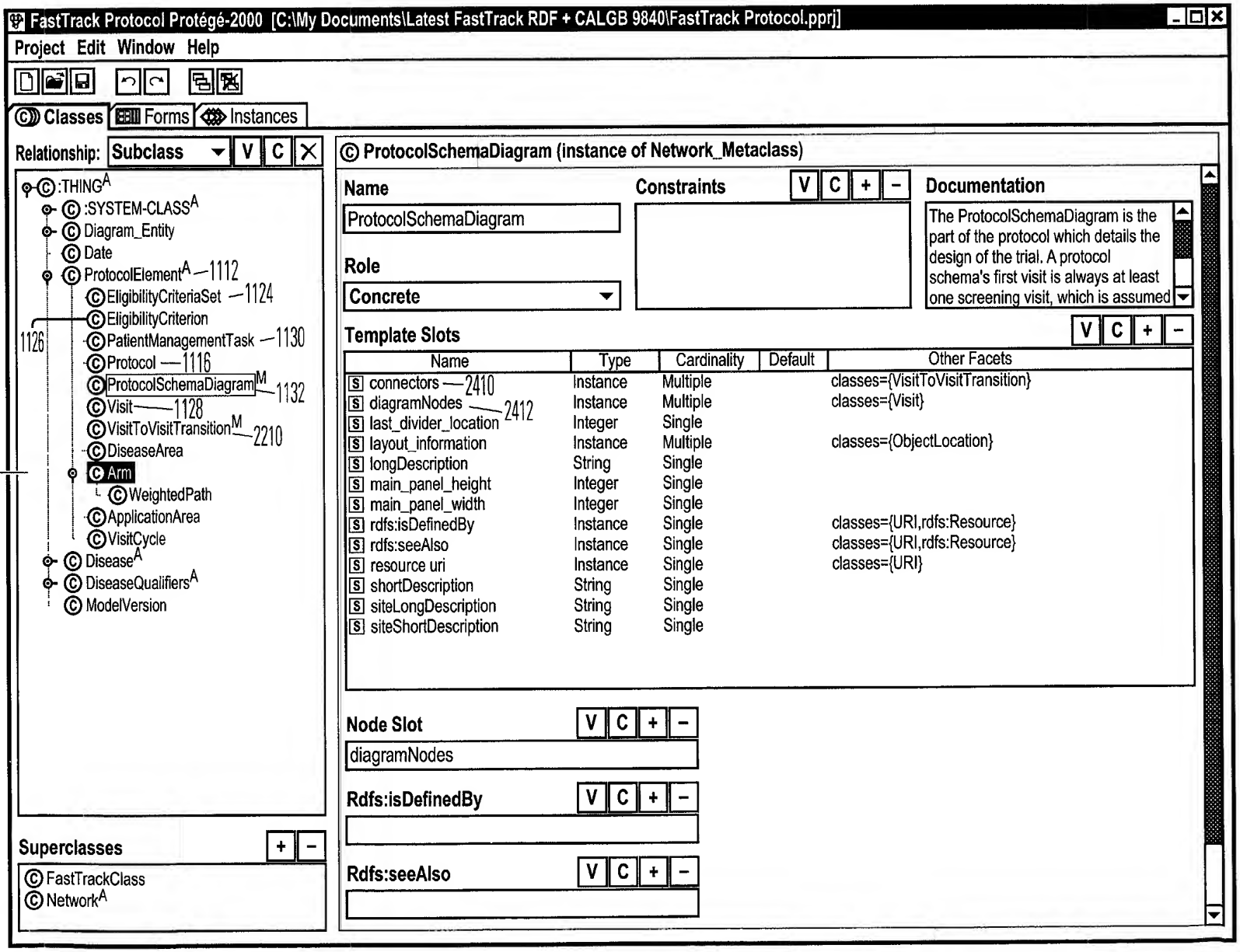

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass V C
:THING A
:SYSTEM-CLASS A
Diagram_Entity
Date
ProtocolElement A 1112
EligibilityCriteriaSet 1124
EligibilityCriterion
PatientManagementTask 1130
Protocol 1116
ProtocolSchemaDiagram M 1132
Visit 1128
VisitToVisitTransition M 2210
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease A
DiseaseQualifiers A
ModelVersion
1126
1110
Superclasses
FastTrackClass
Network A
ProtocolSchemaDiagram (instance of Network_Metaclass)
Name
ProtocolSchemaDiagram
Role
Concrete
Constraints
Documentation
The ProtocolSchemaDiagram is the part of the protocol which details the design of the trial. A protocol schema's first visit is always at least one screening visit, which is assumed
Template Slots
Name | Type | Cardinality | Default | Other Facets
connectors 2410 | Instance | Multiple | | classes={VisitToVisitTransition}
diagramNodes 2412 | Instance | Multiple | | classes={Visit}
last_divider_location | Integer | Single | |
layout_information | Instance | Multiple | | classes={ObjectLocation}
longDescription | String | Single | |
main_panel_height | Integer | Single | |
main_panel_width | Integer | Single | |
rdfs:isDefinedBy | Instance | Single | | classes={URI,rdfs:Resource}
rdfs:seeAlso | Instance | Single | | classes={URI,rdfs:Resource}
resource uri | Instance | Single | | classes={URI}
shortDescription | String | Single | |
siteLongDescription | String | Single | |
siteShortDescription | String | Single | |
Node Slot
diagramNodes
Rdfs:isDefinedBy
Rdfs:seeAlso

FIG. 24

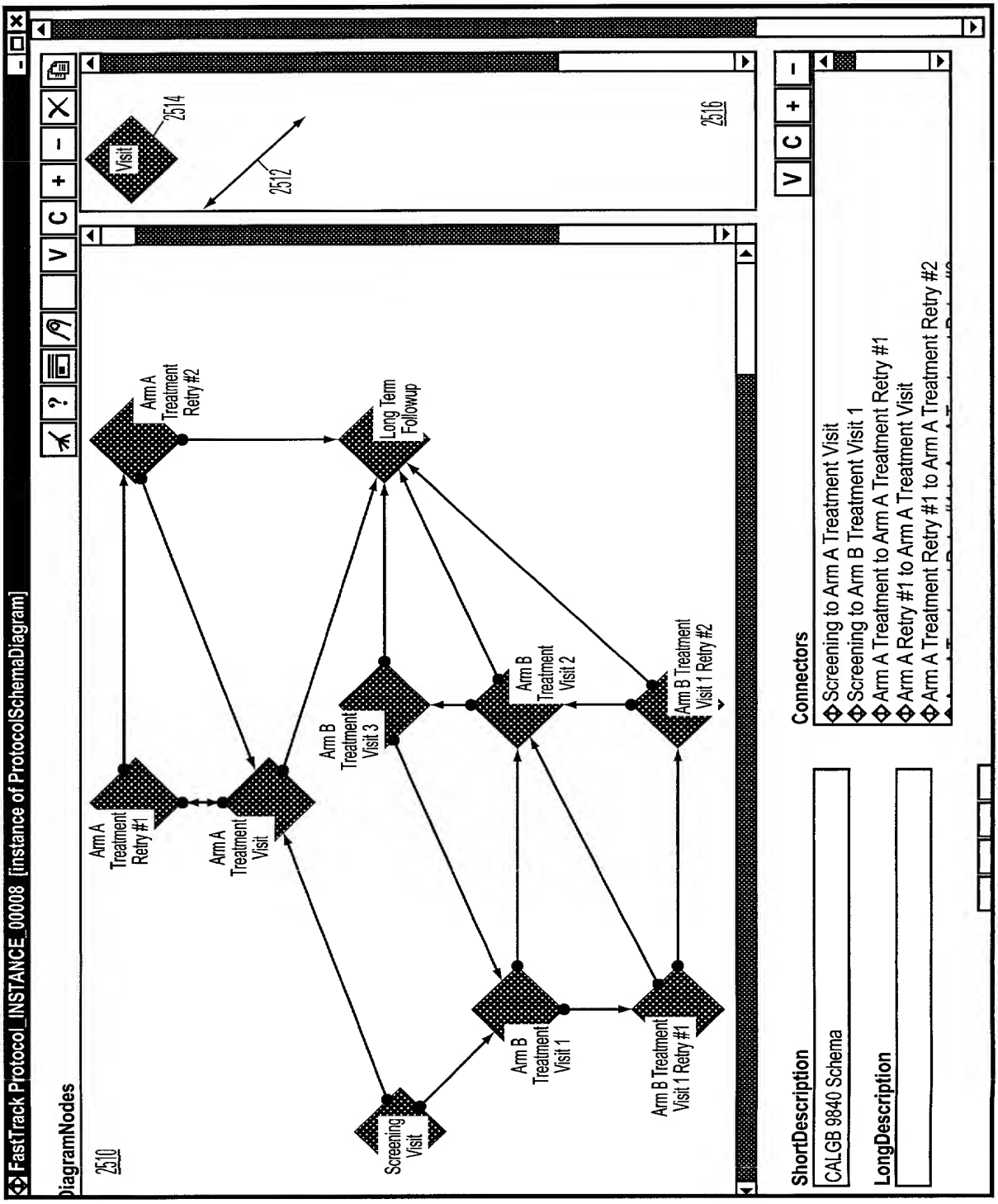

FastTrack Protocol_INSTANCE_00008 [instance of ProtocolSchemaDiagram]
DiagramNodes
2510
Arm A Treatment Retry #1
Arm A Treatment Visit
Arm A Treatment Retry #2
Long Term Followup
Arm B Treatment Visit 3
Arm B Treatment Visit 2
Arm B Treatment Visit 1 Retry #2
Screening Visit
Arm B Treatment Visit 1
Arm B Treatment Visit 1 Retry #1
2512
2514
Visit
2516
V
C
Connectors
Screening to Arm A Treatment Visit
Screening to Arm B Treatment Visit 1
Arm A Treatment to Arm A Treatment Retry #1
Arm A Retry #1 to Arm A Treatment Visit
Arm A Treatment Retry #1 to Arm A Treatment Retry #2
ShortDescription
CALGB 9840 Schema
LongDescription

FIG. 25

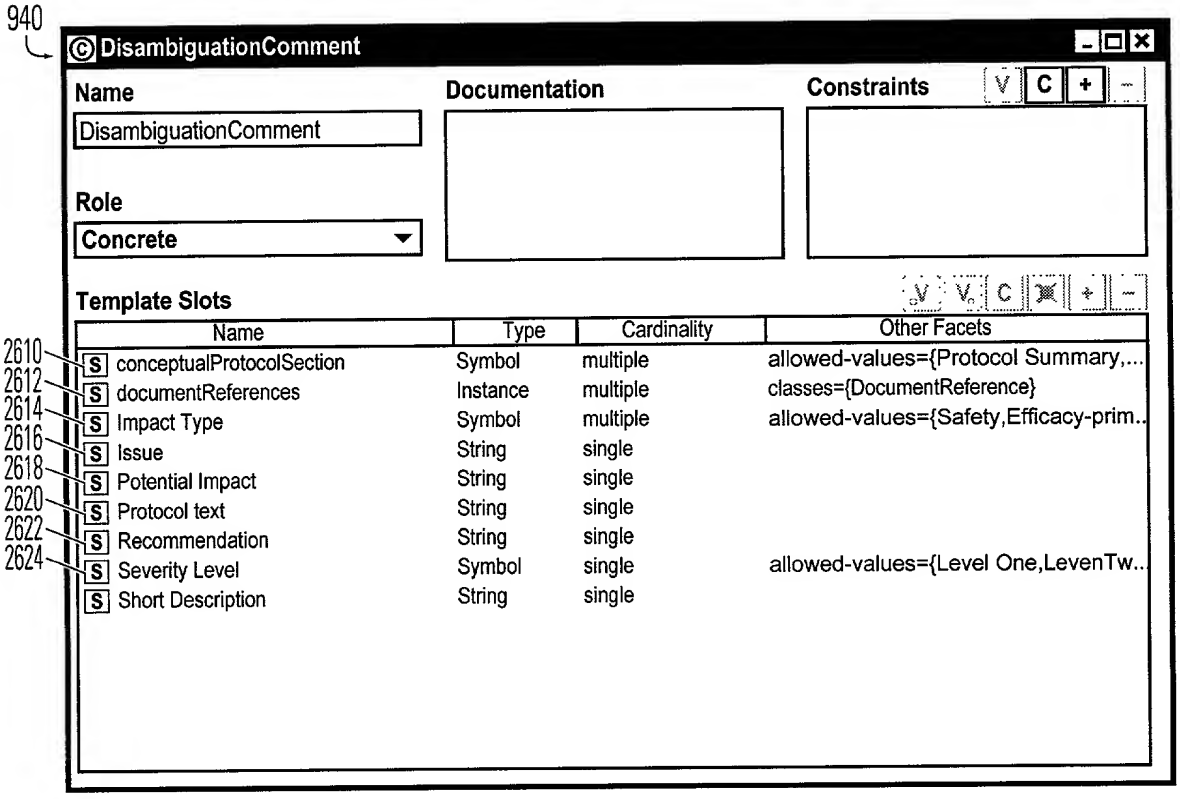

940
DisambiguationComment
Name
DisambiguationComment
Documentation
Constraints
Role
Concrete
Template Slots
Name
Type
Cardinality
Other Facets
2610
conceptualProtocolSection
Symbol
multiple
allowed-values={Protocol Summary,...
2612
documentReferences
Instance
multiple
classes={DocumentReference}
2614
Impact Type
Symbol
multiple
allowed-values={Safety,Efficacy-prim..
2616
Issue
String
single
2618
Potential Impact
String
single
2620
Protocol text
String
single
2622
Recommendation
String
single
2624
Severity Level
Symbol
single
allowed-values={Level One,LevenTw..
Short Description
String
single

FIG. 26

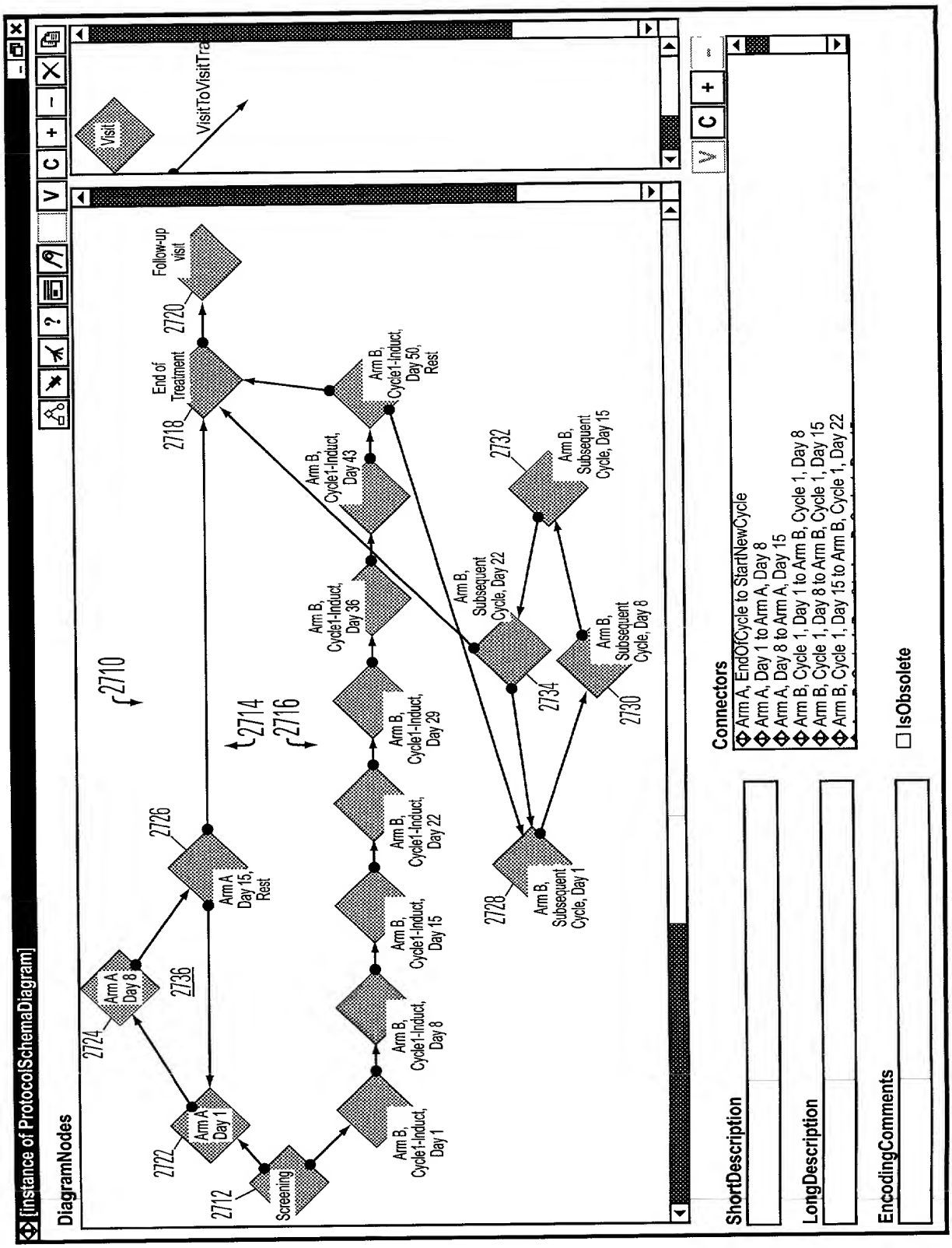

[instance of ProtocolSchemaDiagram]
DiagramNodes
2710
2712
Screening
2714
2716
2718
End of Treatment
2720
Follow-up visit
2722
Arm A Day 1
2724
Arm A Day 8
2726
Arm A Day 15, Rest
2728
Arm B, Subsequent Cycle, Day 1
2730
Arm B, Subsequent Cycle, Day 8
2732
Arm B, Subsequent Cycle, Day 15
2734
Arm B, Subsequent Cycle, Day 22
2736
Arm B, Cycle1-Induct, Day 1
Arm B, Cycle1-Induct, Day 8
Arm B, Cycle1-Induct, Day 15
Arm B, Cycle1-Induct, Day 22
Arm B, Cycle1-Induct, Day 29
Arm B, Cycle1-Induct, Day 36
Arm B, Cycle1-Induct, Day 43
Arm B, Cycle1-Induct, Day 50, Rest
Visit
VisitToVisitTra
Connectors
Arm A, EndOfCycle to StartNewCycle
Arm A, Day 1 to Arm A, Day 8
Arm A, Day 8 to Arm A, Day 15
Arm B, Cycle 1, Day 1 to Arm B, Cycle 1, Day 8
Arm B, Cycle 1, Day 8 to Arm B, Cycle 1, Day 15
Arm B, Cycle 1, Day 15 to Arm B, Cycle 1, Day 22
ShortDescription
LongDescription
EncodingComments
IsObsolete

FIG. 27

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

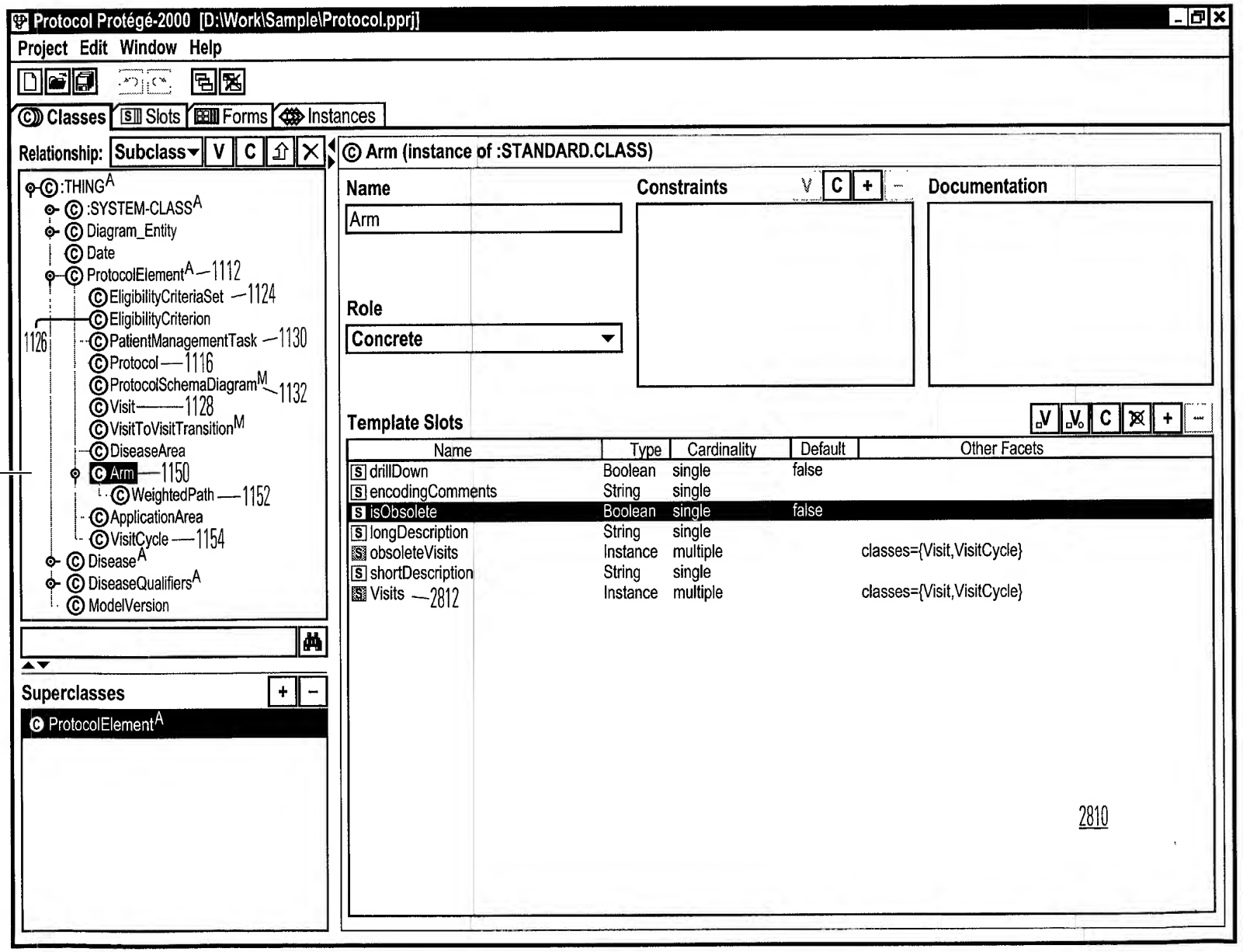


FIG. 28

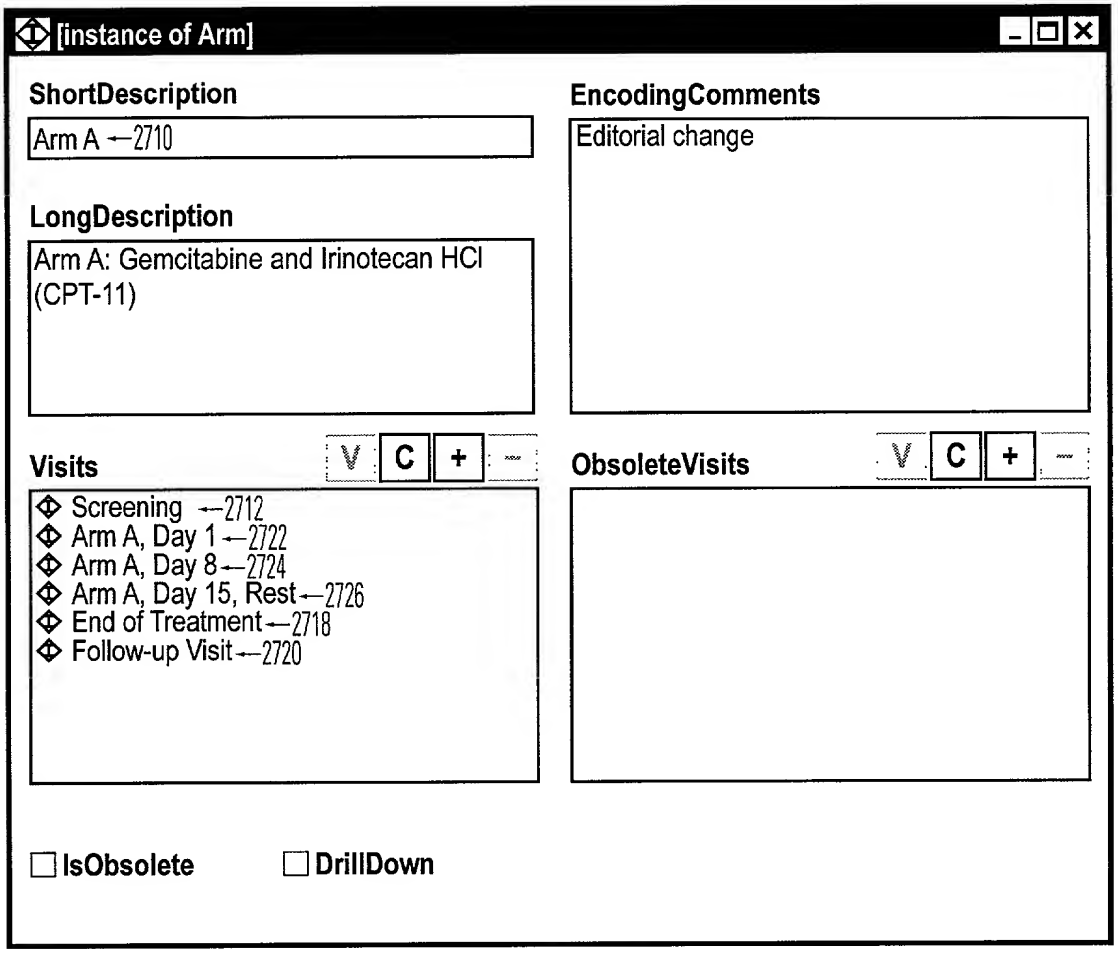

[instance of Arm]
ShortDescription
Arm A ←2710
EncodingComments
Editorial change
LongDescription
Arm A: Gemcitabine and Irinotecan HCl (CPT-11)
Visits
V
C
+
–
Screening ←2712
Arm A, Day 1 ←2722
Arm A, Day 8 ←2724
Arm A, Day 15, Rest ←2726
End of Treatment ←2718
Follow-up Visit ←2720
ObsoleteVisits
V
C
+
–
IsObsolete
DrillDown

FIG. 29

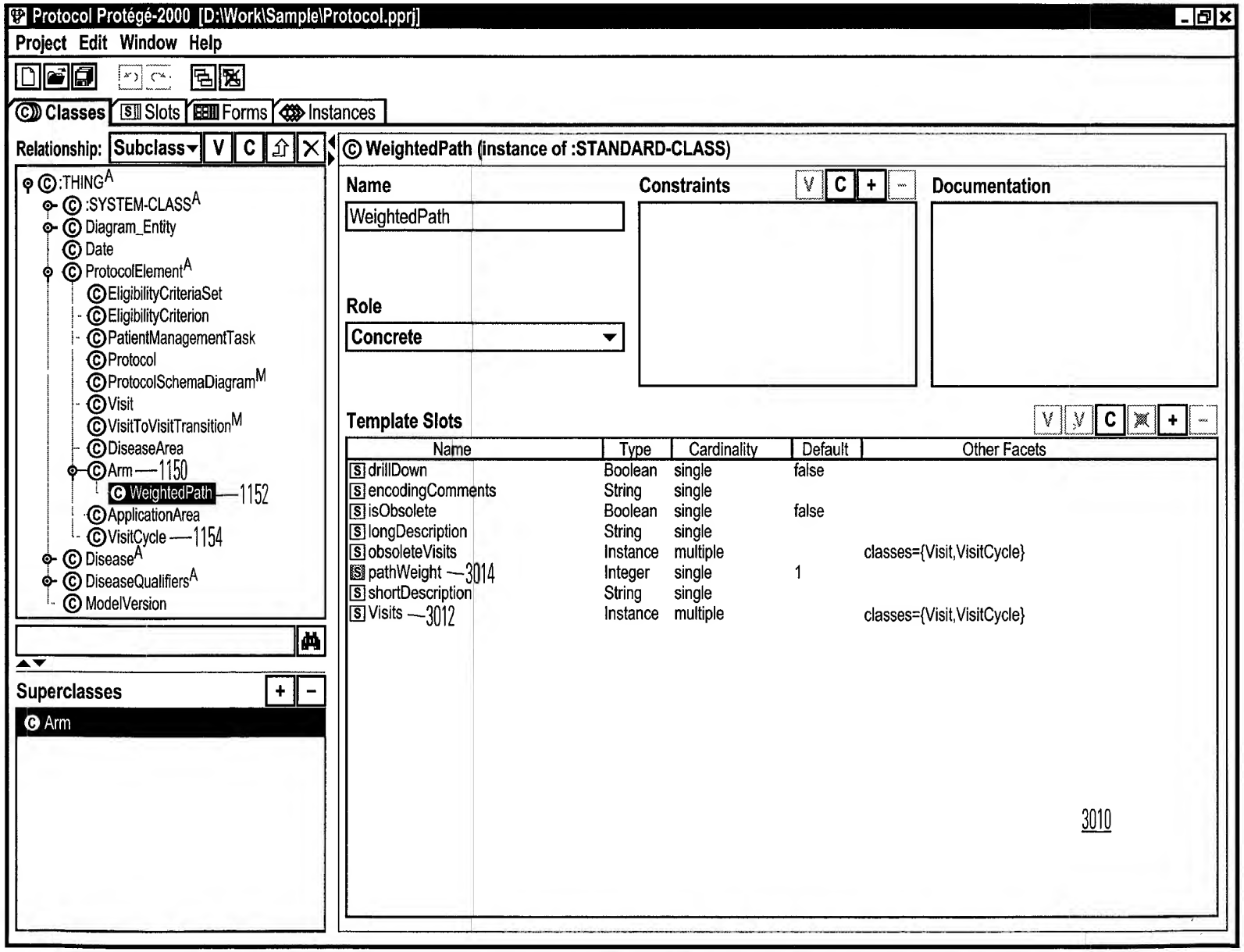


FIG. 30

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

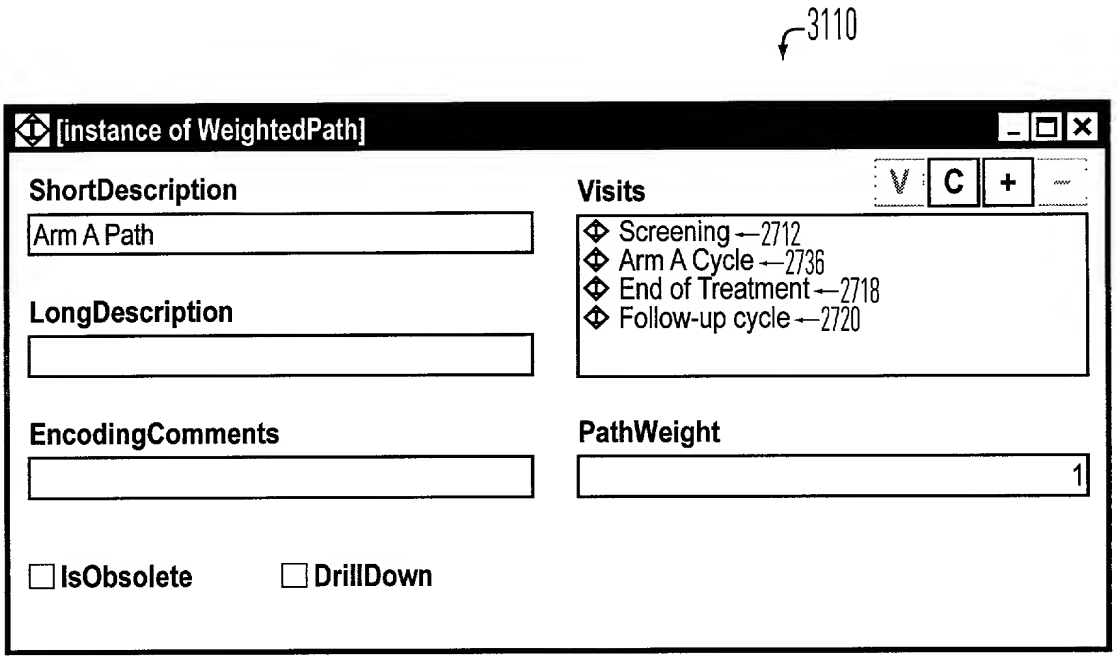

3110
[instance of WeightedPath]
ShortDescription
Arm A Path
LongDescription
EncodingComments
Visits
V
C
+
Screening
2712
Arm A Cycle
2736
End of Treatment
2718
Follow-up cycle
2720
PathWeight
1
IsObsolete
DrillDown

FIG. 31

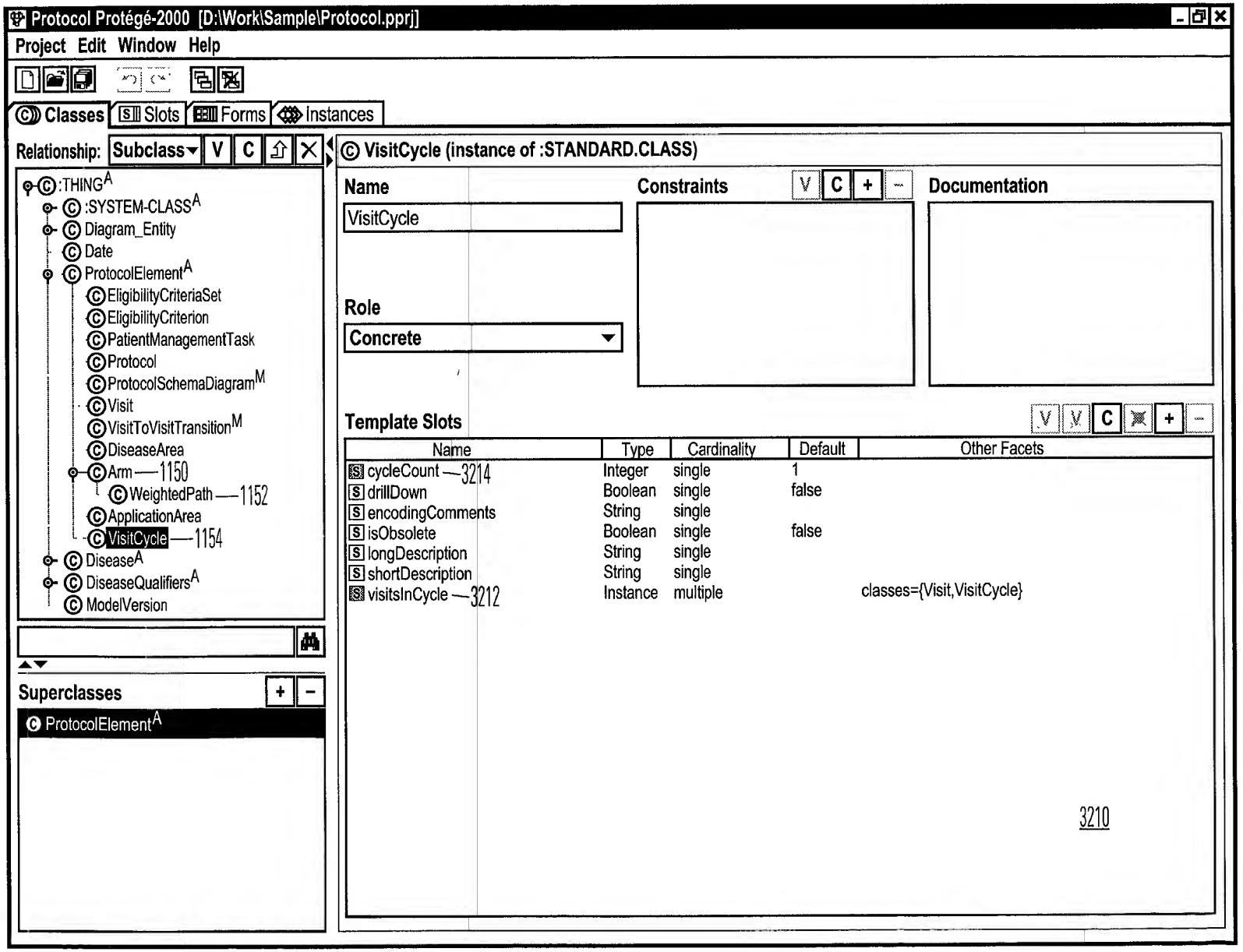

Protocol Protégé-2000 [D:\Work\Sample\Protocol.pprj]
Project Edit Window Help
Classes
Slots
Forms
Instances
Relationship: Subclass
:THING
:SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
1150
WeightedPath
1152
ApplicationArea
VisitCycle
1154
Disease
DiseaseQualifiers
ModelVersion
Superclasses
ProtocolElement
VisitCycle (instance of :STANDARD.CLASS)
Name
VisitCycle
Role
Concrete
Constraints
Documentation
Template Slots
Name
Type
Cardinality
Default
Other Facets
cycleCount
3214
Integer
single
1
drillDown
Boolean
single
false
encodingComments
String
single
isObsolete
Boolean
single
false
longDescription
String
single
shortDescription
String
single
visitsInCycle
3212
Instance
multiple
classes={Visit,VisitCycle}
3210

FIG. 32

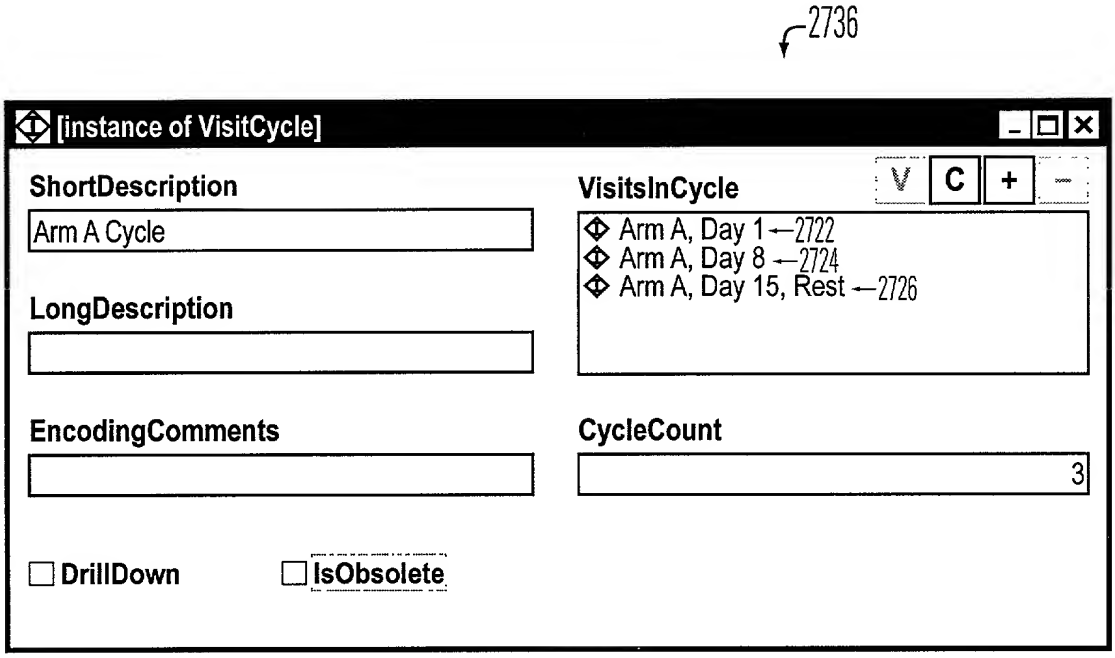

2736
[instance of VisitCycle]
ShortDescription
Arm A Cycle
LongDescription
EncodingComments
VisitsInCycle
V
C
+
–
Arm A, Day 1 2722
Arm A, Day 8 2724
Arm A, Day 15, Rest 2726
CycleCount
3
DrillDown
IsObsolete

FIG. 33

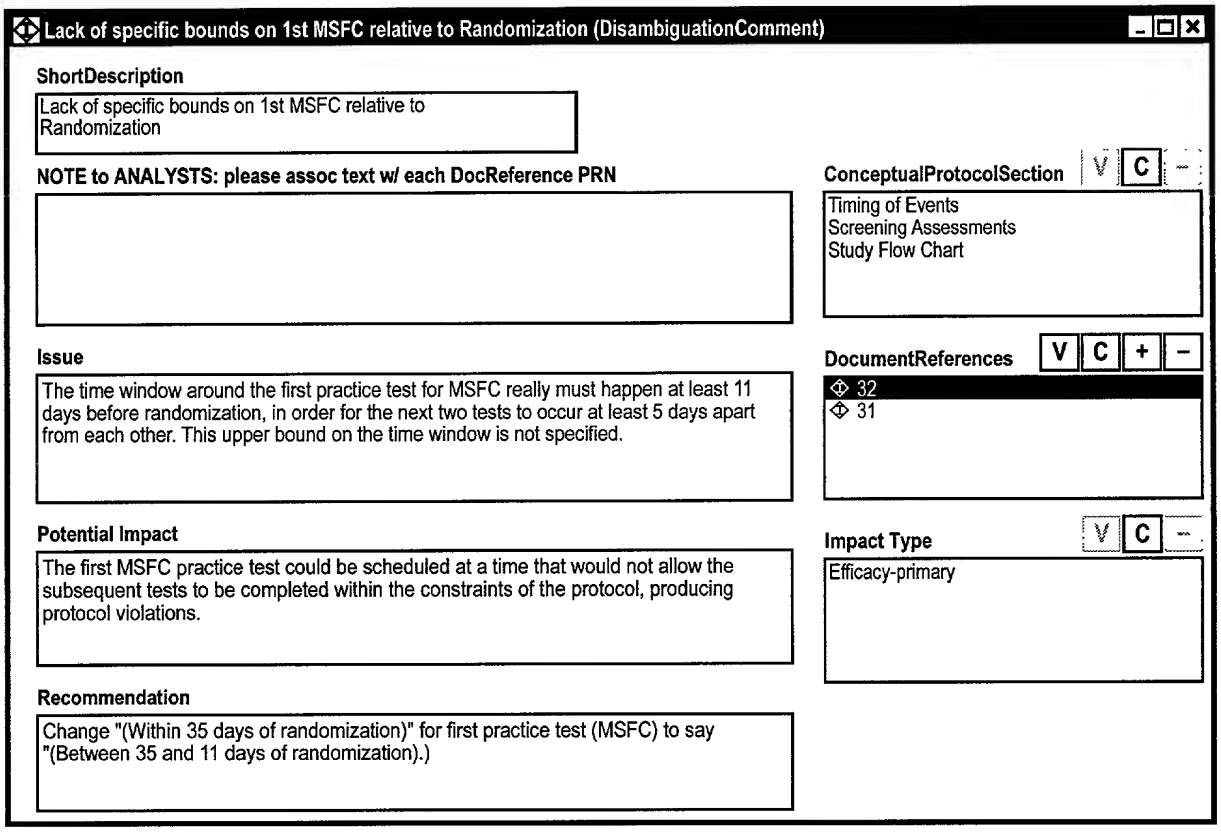


FIG. 34

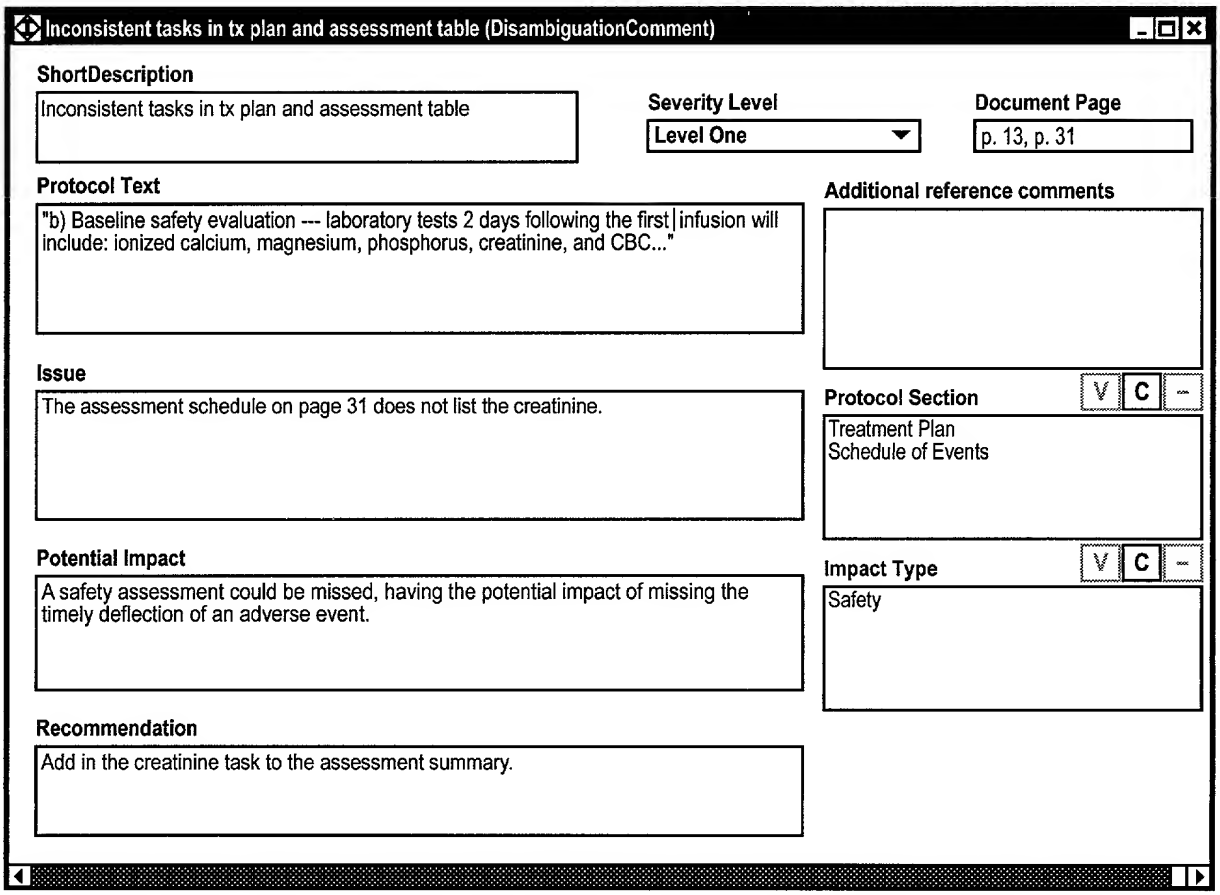

Inconsistent tasks in tx plan and assessment table (DisambiguationComment)
ShortDescription
Inconsistent tasks in tx plan and assessment table
Severity Level
Level One
Document Page
p. 13, p. 31
Protocol Text
"b) Baseline safety evaluation --- laboratory tests 2 days following the first infusion will include: ionized calcium, magnesium, phosphorus, creatinine, and CBC..."
Additional reference comments
Issue
The assessment schedule on page 31 does not list the creatinine.
Protocol Section
V
C
Treatment Plan
Schedule of Events
Potential Impact
A safety assessment could be missed, having the potential impact of missing the timely deflection of an adverse event.
Impact Type
V
C
Safety
Recommendation
Add in the creatinine task to the assessment summary.

FIG. 35

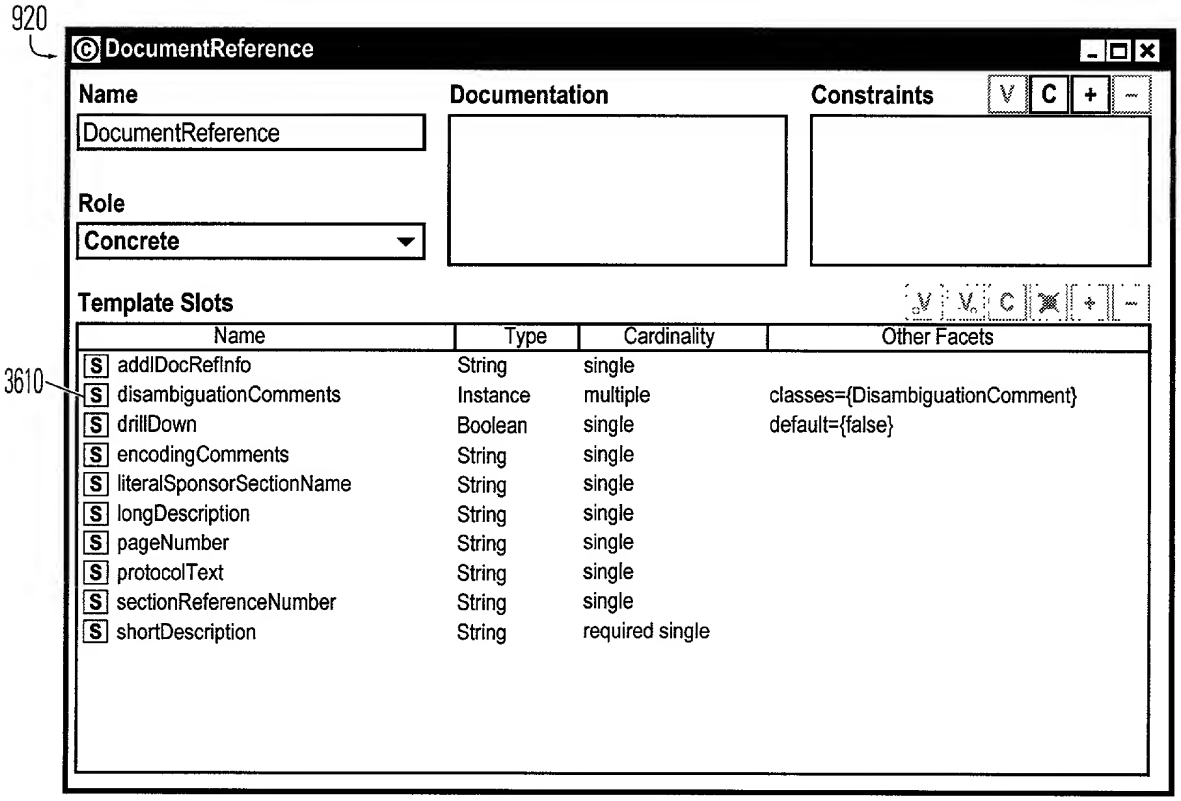

920
DocumentReference
Name
DocumentReference
Documentation
Constraints
V
C
+
-
Role
Concrete
Template Slots
3610
Name
Type
Cardinality
Other Facets
S addlDocRefInfo String single
S disambiguationComments Instance multiple classes={DisambiguationComment}
S drillDown Boolean single default={false}
S encodingComments String single
S literalSponsorSectionName String single
S longDescription String single
S pageNumber String single
S protocolText String single
S sectionReferenceNumber String single
S shortDescription String required single

FIG. 36

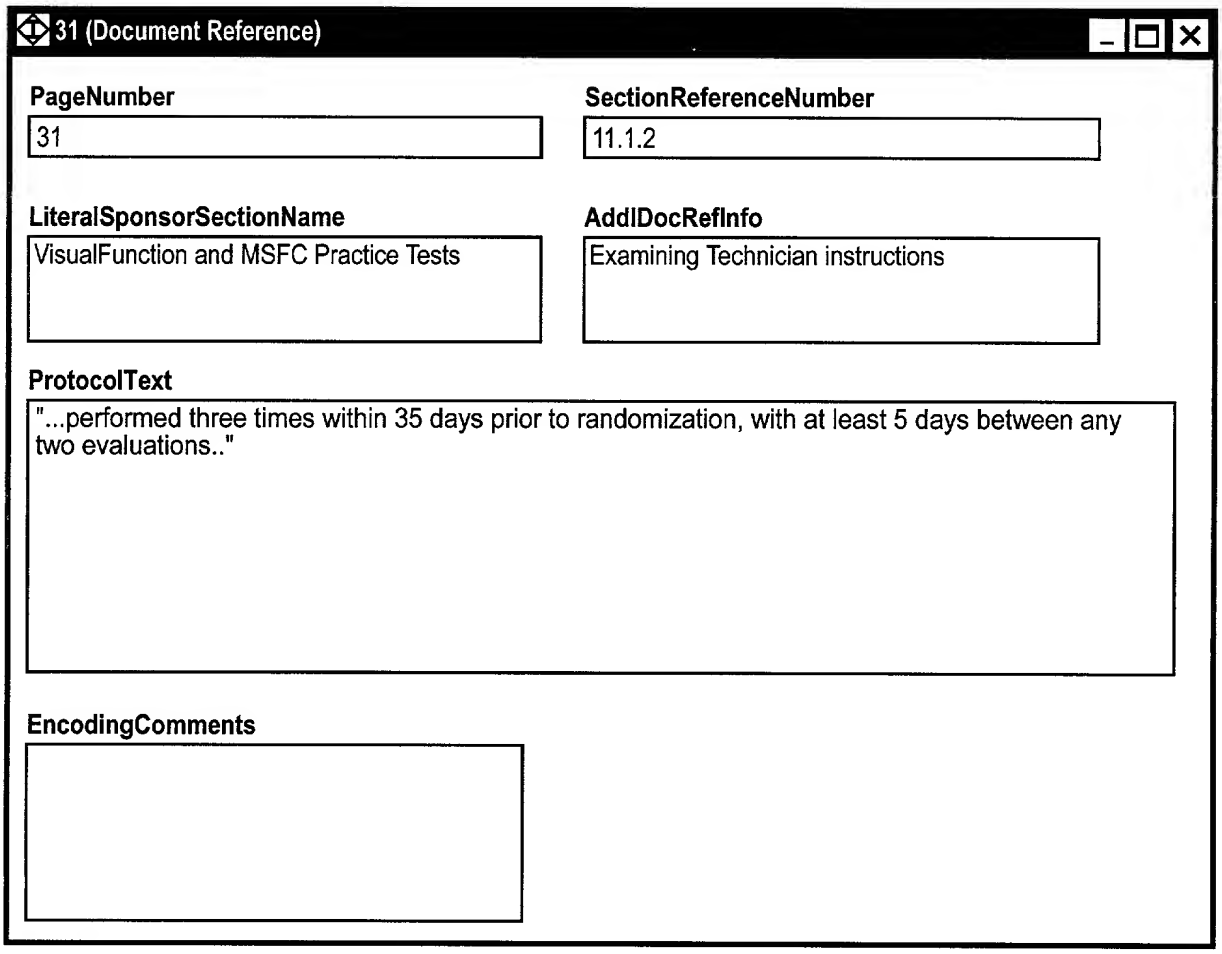

31 (Document Reference)
PageNumber
31
SectionReferenceNumber
11.1.2
LiteralSponsorSectionName
VisualFunction and MSFC Practice Tests
AddlDocRefInfo
Examining Technician instructions
ProtocolText
"...performed three times within 35 days prior to randomization, with at least 5 days between any two evaluations.."
EncodingComments

FIG. 37

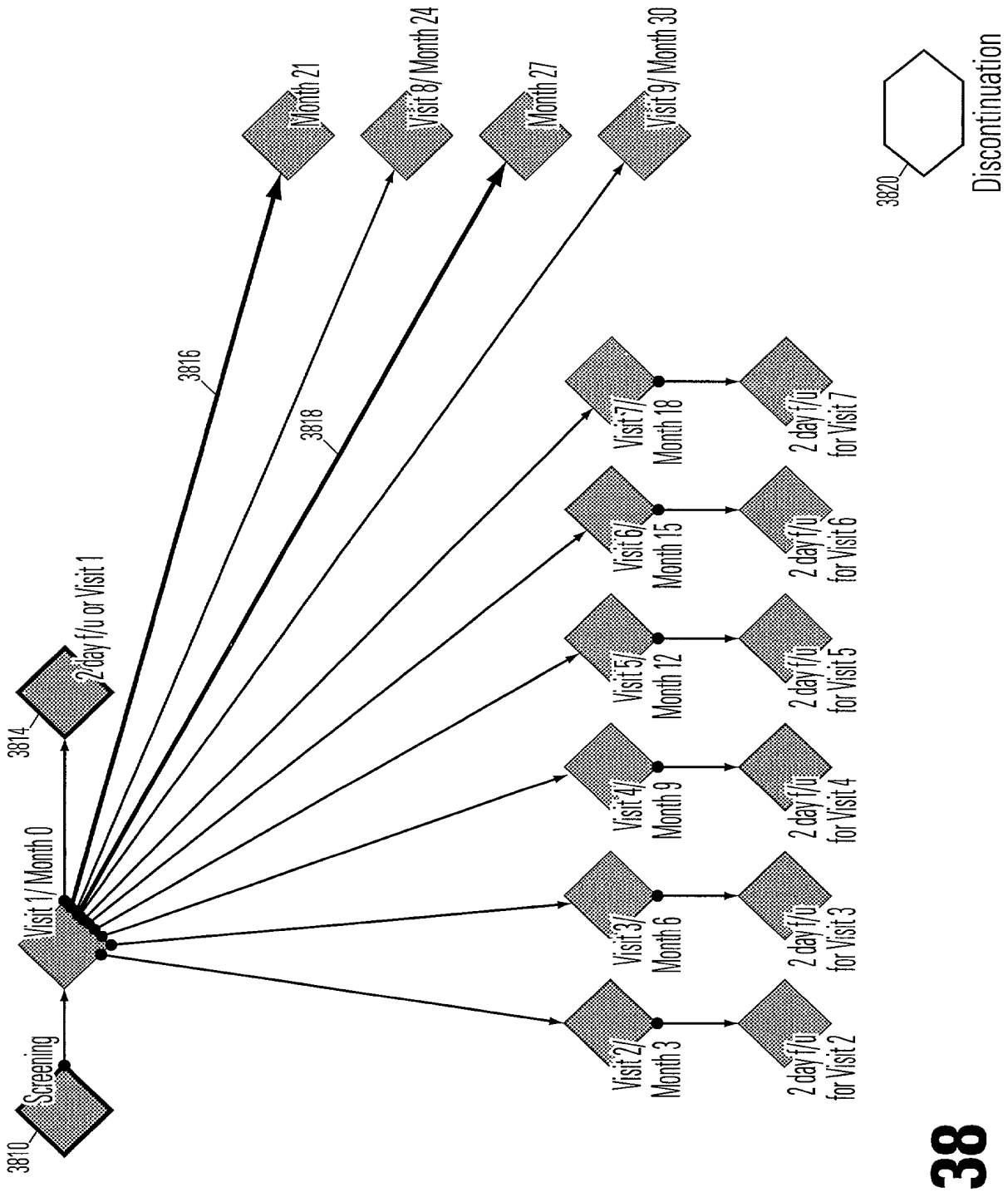

3810
Screening
3814
2 day f/u or Visit 1
Visit 1 / Month 0
3816
3818
Visit 2/
Month 3
Visit 3/
Month 6
Visit 4/
Month 9
Visit 5/
Month 12
Visit 6/
Month 15
Visit 7/
Month 18
Month 21
Visit 8/ Month 24
Month 27
Visit 9/ Month 30
2 day f/u
for Visit 2
2 day f/u
for Visit 3
2 day f/u
for Visit 4
2 day f/u
for Visit 5
2 day f/u
for Visit 6
2 day f/u
for Visit 7
3820
Discontinuation

FIG. 38

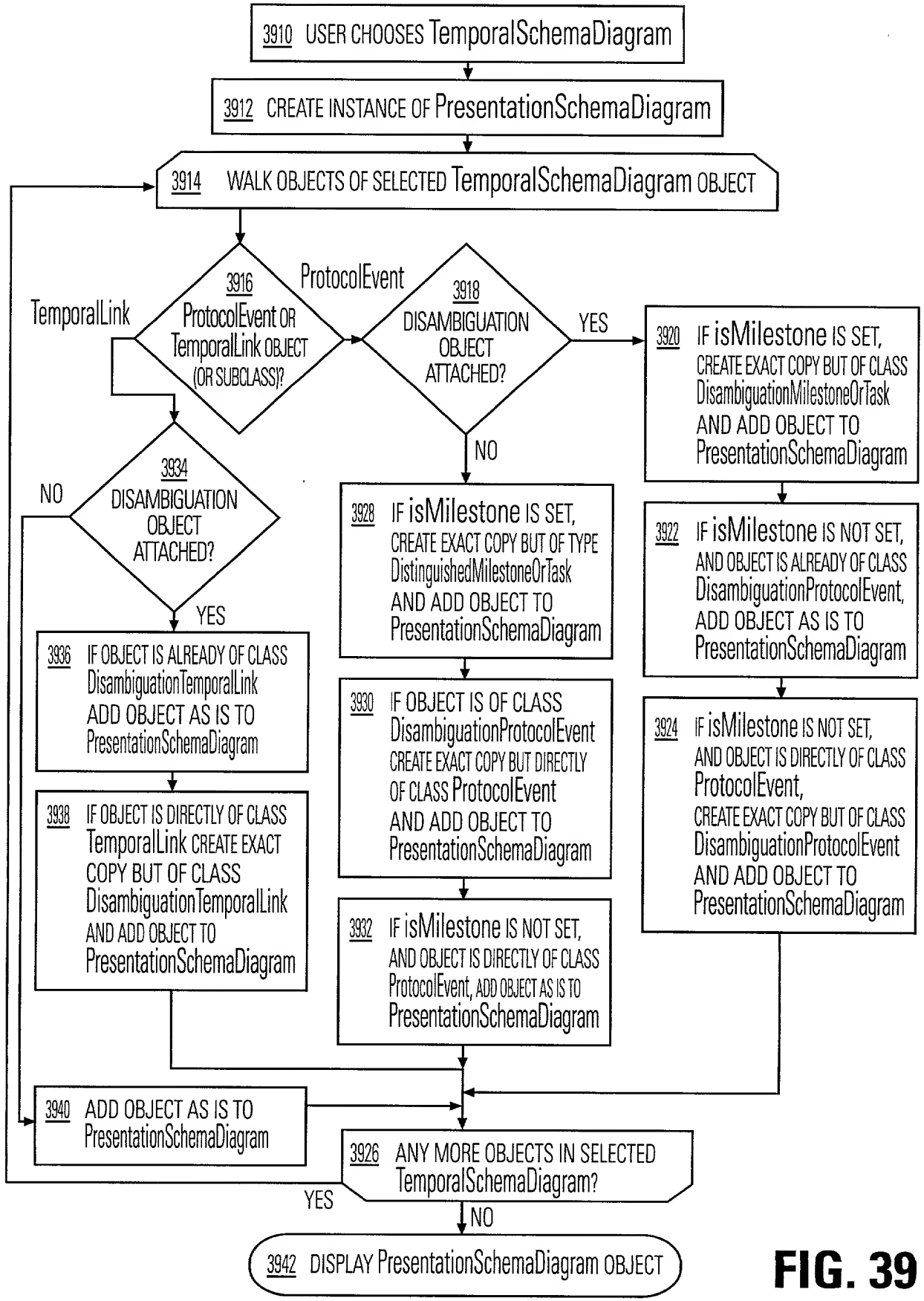

3910 USER CHOOSES TemporalSchemaDiagram
3912 CREATE INSTANCE OF PresentationSchemaDiagram
3914 WALK OBJECTS OF SELECTED TemporalSchemaDiagram OBJECT
3916 ProtocolEvent OR TemporalLink OBJECT (OR SUBCLASS)?
ProtocolEvent
TemporalLink
3918 DISAMBIGUATION OBJECT ATTACHED?
YES
NO
3920 IF isMilestone IS SET, CREATE EXACT COPY BUT OF CLASS DisambiguationMilestoneOrTask AND ADD OBJECT TO PresentationSchemaDiagram
3922 IF isMilestone IS NOT SET, AND OBJECT IS ALREADY OF CLASS DisambiguationProtocolEvent, ADD OBJECT AS IS TO PresentationSchemaDiagram
3924 IF isMilestone IS NOT SET, AND OBJECT IS DIRECTLY OF CLASS ProtocolEvent, CREATE EXACT COPY BUT OF CLASS DisambiguationProtocolEvent AND ADD OBJECT TO PresentationSchemaDiagram
3928 IF isMilestone IS SET, CREATE EXACT COPY BUT OF TYPE DistinguishedMilestoneOrTask AND ADD OBJECT TO PresentationSchemaDiagram
3930 IF OBJECT IS OF CLASS DisambiguationProtocolEvent CREATE EXACT COPY BUT DIRECTLY OF CLASS ProtocolEvent AND ADD OBJECT TO PresentationSchemaDiagram
3932 IF isMilestone IS NOT SET, AND OBJECT IS DIRECTLY OF CLASS ProtocolEvent, ADD OBJECT AS IS TO PresentationSchemaDiagram
3934 DISAMBIGUATION OBJECT ATTACHED?
NO
YES
3936 IF OBJECT IS ALREADY OF CLASS DisambiguationTemporalLink ADD OBJECT AS IS TO PresentationSchemaDiagram
3938 IF OBJECT IS DIRECTLY OF CLASS TemporalLink CREATE EXACT COPY BUT OF CLASS DisambiguationTemporalLink AND ADD OBJECT TO PresentationSchemaDiagram
3940 ADD OBJECT AS IS TO PresentationSchemaDiagram
3926 ANY MORE OBJECTS IN SELECTED TemporalSchemaDiagram?
YES
NO
3942 DISPLAY PresentationSchemaDiagram OBJECT

FIG. 39

DISAMBIGUATION FINDINGS

Item	Impact Type	Protocol Section	Description	Document Reference
1	Safety Efficacy-primary Efficacy-secondary	Protocol Summary Study Flow Chart	**Issue:** The description in the Protocol Synopsis of when assessments should be performed after 16 weeks is not consistent with Appendix I Schedule of Assessments. **Potential Impact:** Confusion as to when to perform these evaluations (clinical parameters and safety assessments) could result in inconsistent and inaccurate collection of data for the study. **Recommendation:** Revise sentence in the Protocol Synopsis to read, "After 16 weeks these evaluations will be performed every two to "four" months..." in order to be consistent with the timepoints indicated in Appendix I Schedule of Assessments.	*Pg. 12; Section Protocol Synopsis; Procedure; Paragraph 6:* "Clinical parameters (ACR core set) and safety assessments (adverse events and laboratory parameters) will be performed at baseline and then at monthly intervals up to 16 weeks. After 16 weeks these evaluations will be performed every two to three months, up to 104 weeks."

FIG. 40

Item	Impact Type	Protocol Section	Description	Document Reference
4	Safety Accrual	Screening Assessments Study Flow Chart	**Issue:** The protocol text specifies that if an analysis with evidence of seropositivity was performed within 6 months before screening, then rheumatoid factor testing will not have to be performed at screening. However, this is not noted in Appendix I Schedule of Assessments. **Potential Impact:** Unnecessary analysis performed at screening. **Recommendation:** Add a footnote to the Rheumatoid Factor assessment in Appendix I to clarify that documented evidence of seropositivity is acceptable as screening data if obtained within 6 months before screening.	*Pg. 28; Section 8.6.2; Rheumatoid Factor:* "Unless there is documented evidence of rheumatoid factor titre within 6 months before screening a blood sample for this analysis will be taken." *Pg. 41; Section Appendix I; Schedule of Assessments*

FIG. 41